Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BASOPHILS: 0.3 % (normal 0 to 1)

[redacted] 20[redacted] CREATININE: 0.37 mg/dL (normal 0.73 to 1.18)

[redacted] 20[redacted] CRP: 11.8 MG/L (normal 0.2 to 5)

[redacted] 20[redacted] Electrocardiogram: Abnormal: Rhythm

[redacted] 20[redacted] EOSINOPHILS: 0.1 % (normal 1 to 5)

[redacted] 20[redacted] FIBRINOGEN: 4.08 G/L (normal 2 to 4.5)

[redacted] 20[redacted] GLUCOSE: 77 mg/dL (normal 70 to 99)

[redacted] 20[redacted] GLUCOSE (URINALYSIS): Negative

[redacted] 20[redacted] HEMATOCRIT: 37.5 % (normal 35 to 45)

[redacted] 20[redacted] IRON: 2.8 umol/l (normal 8.9 to 21.4)

[redacted] 20[redacted] LYMPHOCYTES: 10.6 % (normal 25 to 50)

[redacted] 20[redacted] MONOCYTES: 3.5 % (normal 1 to 11)

[redacted] 20[redacted] NEUTROPHILS: 85.5 % (normal 25 to 60)

[redacted] 20[redacted] PLATELET COUNT: 530 X10**3/MCL (normal 130 to 400)

[redacted] 20[redacted] POTASSIUM: 4.3 MMOL/L (normal 3.8 to 5)

[redacted] 20[redacted] SGOT/AST: 13 U/L (normal 0 to 45)

[redacted] 20[redacted] SGPT/ALT: 10 U/L (normal 0 to 40)

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

[redacted] 20[redacted] SR: 25 MM/HR (normal 3 to 8)

[redacted] 20[redacted] URINE BLOOD: Negative

[redacted] 20[redacted] URINE KETONES: Negative

[redacted] 20[redacted] URINE LEU: 6 uL (normal 0 to 15)

[redacted] 20[redacted] URINE NITR: Negative

[redacted] 20[redacted] URINE PH: 7.5 No units (normal 4.5 to 7.5)

[redacted] 20[redacted] URINE SPECIFIC GRAVITY: 1002 No units (normal 1015 to 1025)

[redacted] 20[redacted] WBC: 15.29 X10**3/MCL (normal 4.5 to 13.5)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD-MPL	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
ASTHMA/REACTIVE AIRWAY DISEASE: BRONCHIAL ASTHMA	20[redacted]
PEPTIC ULCER DISEASE: CHRONIC GASTRITIS. HELICOBACTER PYLORI INFECTION	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
INFLAMMATORY BOWEL DISEASE: ANAL FISSURA	20[redacted]
ANEMIA: SIDEROPENIC ANAEMIA	20[redacted]
MURMUR: HEART MURMUR	20[redacted]
SYNCOPE: EPISODES OF SYNCOPE	20[redacted]
MIGRAINE HEADACHE: HEADACHE, TICKS	20[redacted]
OTHER: LEFT-SIDE CYST OF ETHMOID SINUS	20[redacted]
OTHER: WEIGHT AND HEIGHT DEFICIENCY	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: DENTAL CARIES	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted] / 1	[redacted] / 43	56
MPL	[redacted] / 57	[redacted] / 358	310

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	1000 mg (milligram(s))	BID	Y-M: [redacted]
COLECALCIFEROL	1000 mg (milligram(s))	QD	Y-M: [redacted]
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: [redacted] / -51
POTASSIUM CHLORIDE	391 mg (milligram(s))	QD	Y-M: [redacted] / -51
PREDNISONE	20 mg (milligram(s))	QD	Y-M: [redacted] / -51
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: [redacted] / -48

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SULFASALAZINE	1000 mg (milligram(s))	BID	Y-M: [redacted]	ONGOING
COLECALCIFEROL	1000 mg (milligram(s))	QD	Y-M: [redacted]	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: [redacted] / -48	ONGOING
TRIAMCINOLONE ACETONIDE	1 DF (dosage form)	BID	Y-M: [redacted] / 129	Y-M: [redacted] / 147
BETADERMIC	DOSE - OINTMENT DOSE - OINTMENT	BID	Y-M: [redacted] / 140	Y-M: [redacted] / 147
DITHRANOL	DOSE - OINTMENT OINTMENT - DOSE	BID	Y-M: [redacted] / 140	Y-M: [redacted] / 147
LORINDEN A	DOSE - OINTMENT DOSE - OINTMENT	BID	Y-M: [redacted] / 140	Y-M: [redacted] / 147
PARACETAMOL	500 mg (milligram(s))	QD	Y-M: [redacted] / 144	Y-M: [redacted] / 145

Event #1: Serious Adverse Event

Event Description	PSORIASIS
Preferred term	乾癬
AE Onset Date / Rx Day	[redacted] / 128
Age at AE Onset	[redacted]
Laboratory Testing	

NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	147
Duration of AE	20 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).

FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の乾癬を発現した。関連する病歴は，潰瘍性大腸炎であった。
本試験では，すべての被験者が最初の 8 週間にアダリムマブの投与を受け，投与 8 週時に維持療法期アダリムマブ高用量，維持療法期アダリムマブ標準用量又はプラセボのいずれかに無作為に割り付けられた。
20[redacted] 年 [redacted] 月 [redacted] 日，乾癬が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，乾癬は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，投与 18 週時の規定来院で乾癬と診断された。同日，被験者は救急で皮膚科医の診察を受けるため，待機的に入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は管理上の理由のため退院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は皮膚科クリニックに再入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Lorinden A，アセトアミノフェン，Diprosalic，Mediderm 及び Cygnoline ointment 1/16-1/8%が投与された。

The patient's past medications include:

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

Causality for HUMIRA (Blinded)

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1) Psoriasis (10037153) (Psoriasis (10037153)) [v.21.1] [10037153]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of PSORIASIS

- Investigator: Not applicable

- AbbVie: Not applicable

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
消化不良	X			

Treatment Group	Age at Study Start	Sex	Race
IHD-MHD	1[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANAEMIA	20[redacted]
OBESITY: OBESITY	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: STREPTOCOCCUS ALLERGISATION	20[redacted]
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	20[redacted]
OTHER: VITAMIN D3 DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MHD	[redacted]0[redacted] / 57	[redacted]20[redacted] / 358	308

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
COLECALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted]-[redacted] / -161
MESALAZINE	1500 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -161
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -45
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -27

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
COLECALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted]-[redacted] / 161	- ONGOING
MESALAZINE	1500 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 161	- ONGOING
ELECTROLYTE SOLUTIONS	500 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 364	Y-M: 20[redacted]-[redacted] / 364
GLUCOSE	20 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 364	Y-M: 20[redacted]-[redacted] / 364
RECTANAL	150 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 364	Y-M: 20[redacted]-[redacted] / 365
ELECTROLYTE SOLUTIONS	250 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 365	Y-M: 20[redacted]-[redacted] / 365

Event #1: Serious Adverse Event

Event Description	FUNCTIONAL DYSPEPSIA
Preferred term	消化不良
AE Onset Date / Rx Day	[redacted]20[redacted] / 364 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 365): GASTRODUODENOSCOPY: NORMAL PICTURE OF THE ESOPHAGUS, STOMACH AND DUODENUM

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FUNCTIONAL DYSPEPSIA PROBABLY AFTER DIETETICAL MISTAKE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second

disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の機能性ディスペプシアを発現した。関連する病歴は，肥満，潰瘍性大腸炎，レンサ球菌のアレルギー化及びクロストリジウム・ディフィシレ感染であった。被験者は非喫煙者及び非アルコール摂取者であった。
20[redacted] 年 [redacted] 月 [redacted] 日，機能性ディスペプシアが発現した。20[redacted] 年 [redacted] 月 [redacted] 日，機能性ディスペプシアは回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，おそらく「誤食（dietetical mistake）」に関連した上腹部痛のため入院した。上部消化管内視鏡検査が実施され，結果は正常であったが，機能性ディスペプシアの診断が下された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

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

METRONIDAZOL for EXACERBATION OF ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

METRONIDAZOL for EXACERBATION OF ULCERATIVE COLITIS

Causality for HUMIRA (Blinded)

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1) Functional dyspepsia (10064536) (Dyspepsia (10013946)) [v.22.0] [10064536]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of FUNCTIONAL DYSPEPSIA

- Investigator: Functional dyspepsia probably after dietetical mistake.

- AbbVie: Development of the event is not consistent with study drug's mechanism of action. Additionally the event appears to be related to dietary choices.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] GASTRODUODENOSCOPY: Normal picture of the esophagus, stomach and duodenum.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD-MHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
FEEDING DISORDERS/DIETARY INTOLERANCES: LACTOSE INTOLERANCE	20[redacted]
GASTROINTESTINAL BLEED: RECTAL BLEEDING	20[redacted]
OTHER: VITAMIN D3 DEFICIENCY	20[redacted]
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MHD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	308

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
COLECALCIFEROL	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -224
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -133
AZATHIOPRINE	37.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -45
METHYLPREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -42
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / -27

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
COLECALCIFEROL	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -224	ONGOING
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -133	ONGOING
AZATHIOPRINE	37.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -45	ONGOING
LEVOCETIRIZINE DIHYDROCHLORIDE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 287
AMBROXOL HYDROCHLORIDE	15 mg (milligram(s))	BID	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 292
ANDROGRAPHIS PANICULATA LEAF W/GENTIANA SPP.	1 DF (dosage form)	QD	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 292
SODIUM CHLORIDE	2 DF (dosage form)	BID	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 292
CIRRUS	5 mg (milligram(s))	BID	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 308
MOMETASONE FUROATE	50 mcg (microgram(s))	BID	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 308

Event #1: Serious Adverse Event

Event Description	FRACTURE OF THE PROXIMAL PHALANX OF THE 5TH FINGER OF THE LEFT PALMA WITH THE TRANSLOCATION
Preferred term	手骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 315
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 315): SURGERY - INTRODUCTION OF THE KIRSCHNER WIRE: [redacted]20[redacted] - SURGERY (REMOVAL OF THE KIRSCHNER WIRE

AE Stopped Rx Day	346
Duration of AE	32 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	TRAUMA WITH FOOTBALL BALL
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).

FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の変位を伴う左手掌第 5 指基節骨骨折を発現した。関連する病歴は，ビタミン D3 欠乏及び潰瘍性大腸炎（左側）であった。被験者は非喫煙者であり，飲酒の習慣はなかった。
20[redacted] 年 [redacted] 月 [redacted] 日，変位を伴う左手掌第 5 指基節骨骨折が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，変位を伴う左手掌第 5 指基節骨骨折は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，骨折部位の固定のため，キルシュナー鋼線刺入術を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は再入院した。20[redacted] 年 [redacted] 月 [redacted] 日，骨折部位の固定を解除し，キルシュナー鋼線を外科的に抜去した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for HUMIRA (Blinded)

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1) Fractured finger (10017286) (Hand fracture (10019114)) [v.21.0] [10017286]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for HUMIRA (Blinded)

Event of FRACTURE OF THE PROXIMAL PHALANX OF THE 5TH FINGER OF THE LEFT PALMA WITH THE TRANSLOCATION

- Investigator: TRAUMA WITH FOOTBALL BALL

- AbbVie: EVENT IS MORE LIKELY RELATED TO TRAUMATIC INJURY FROM FOOTBALL.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HEMATOCRIT: 32.2 % (normal 35.0 to 45.0)

[redacted] 20[redacted] HEMOGLOBIN: 10.1 G/DL (normal 12 to 15)

[redacted] 20[redacted] PLATELET COUNT: 297 X10**9/L (normal 140 to 420)

[redacted] 20[redacted] RBC (HEMATOLOGY): 4.30 T/l (normal 4.00 to 5.30)

[redacted] 20[redacted] WBC (HEMATOLOGY): 8.44 X10**9/L (normal 4.50 to 13.5)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD	1[redacted]	MALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 40	53

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -87
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -56
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / -56
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -56
COLECALCIFEROL	2 gtt (drop(s))	QD	Y-M: 20[redacted] / -14
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
POTASSIUM CHLORIDE	1 TABLET	QD	Y-M: 20[redacted] / -14
PREDNISONE	5 mg (milligram(s))	QD	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
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -87	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -56	ONGOING
COLECALCIFEROL	2 gtt (drop(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 33
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 33
POTASSIUM CHLORIDE	1 TABLET	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 33
PREDNISONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 33
INFLIXIMAB	250 mg (milligram(s))	OTHER: ACCORDING TO INFLIXIMAB THERAPY RULES	Y-M: 20[redacted] / 58	ONGOING

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 57 (17 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	

NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	81 (41 DAYS AFTER LAST TREATMENT)
Duration of AE	25 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second

disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男児（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められ，同日に被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
20[redacted] 年 [redacted] 月 [redacted] 日（投与 8 週時），被験者は試験を中止した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。
治療薬としてインフリキシマブが投与された。

The patient's past medications include:

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

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

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

KALIPOZ PROLONGATUM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

VITAMINUM D3 for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ULCERATIVE COLITIS FLARE

- Investigator: UC Flare

- AbbVie: The underlying UC

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -318
CICLOSPORIN	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -301
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -289

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / - 289	ONGOING
CIPROFLOXACIN HYDROCHLORIDE	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 56
ENOXAPARIN SODIUM	0.2 mL (millilitre(s))	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 56
SACCHAROMYCES BOULARDII	1 DF (dosage form)	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 56
GLUCOSE	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 48
CICLOSPORIN	150 mg (milligram(s))	QD	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
CICLOSPORIN	350 mg (milligram(s))	OTHER: 200 MG + 150 MG	Y-M: 20[redacted] / 50	ONGOING
GLUCOSE	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 51
RED BLOOD CELLS, CONCENTRATED	300 mL (millilitre(s))	QD	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
FERROUS SULFATE	1 DF (dosage form)	BID	Y-M: 20[redacted] / 56	ONGOING
FOLIC ACID	1 DF (dosage form)	QD	Y-M: 20[redacted] / 56	ONGOING
MAGNESIUM ASPARTATE	1 DF (dosage form)	QD	Y-M: 20[redacted] / 56	ONGOING
VITAMINUM	1 DF (dosage form)	QD	Y-M: 20[redacted] / 56	ONGOING

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

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 47 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	56 (14 DAYS AFTER LAST TREATMENT)
Duration of AE	10 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC FLARE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).

FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，高度の広範囲の潰瘍性大腸炎／汎大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，胃痛及び血便の徴候及び症状が認められたため，被験者は入院した。本事象は，アダリムマブによる生物学的療法の有効性欠如のため発現したものであり，治療薬としてシクロスポリンが投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
関連するリスク因子には原疾患があった。
治療薬としてシプロフロキサシン，Clexan（エノキサパリンナトリウム），ビタミン B 製剤，Enterol，濃厚赤血球，5%ブドウ糖，Asmag，Sorbifer durules（アスコルビン酸／硫酸鉄水和物），Acidum folicum（葉酸）及びシクロスポリンが投与された。

The patient's past medications include:

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

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

Causality for HUMIRA (Open Label)

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1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.19.0] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of UC FLARE

- Investigator: Ulcerative colitis flare.

- AbbVie: The underlying UC.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
SULFASALAZINE	2 TABLETS	QID	Y-M: 20[redacted] / -253
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -243
COLECALCIFEROL	2000 JM	QD	Y-M: 20[redacted] / -14
PICO-SALAX	150 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
FENTANYL	0.075 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
PARACETAMOL	1 g (gram(s))	QD	Y-M: 20[redacted] / -13
PROPOFOL	200 mg (milligram(s))	QD	Y-M: 20[redacted] / -13

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SULFASALAZINE	2 TABLETS	QID	Y-M: 20[redacted] / -253	ONGOING
COLECALCIFEROL	2000 JM	QD	Y-M: 20[redacted] / -14	ONGOING
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -13	ONGOING
FERRIC PYROPHOSPHATE	20 mg (milligram(s))	TID	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
OMEPRAZOLE	1 TABLET	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
POTASSIUM CHLORIDE	1 TABLET	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
BLOOD AND RELATED PRODUCTS	2 DF (dosage form)	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 35

Event #1: Serious Adverse Event

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 29
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	

NOT REPORTED	
AE Stopped Rx Day	36
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNDERLYING DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every

week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number:[redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の貧血を発現した。関連する病歴は，左側潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，貧血が発現した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，ヘモグロビン低値のため輸血が行われ，同日に被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。
治療薬として Actiferol（ピロリン酸第二鉄）が投与された。

The patient's past medications include:

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

ENCORTON for ULCERATIVE COLITIS (Started [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Anemia (10002272) (Anaemia (10002034)) [v.20.1] [10002272]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ANEMIA

- Investigator: UNDERLYING DISEASE

- AbbVie: A COMMON COMPLICATION OF THE UNDERLYING UC

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Rectum/Sigmoid = 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions), Presence of friability - yes

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
頭痛	X			
意識消失	X			

Treatment Group	Age at Study Start	Sex	Race
ISD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
COGNITIVE, BEHAVIORAL OR PSYCHIATRIC DISORDER: BRIEF LOSS OF CONTACT AND ABNORMAL EEG AROUND AGE 5. TX WITH VALPROIC ACID.	20[redacted]
COGNITIVE, BEHAVIORAL OR PSYCHIATRIC DISORDER: ELECTIVE MUTISM	20[redacted]
COGNITIVE, BEHAVIORAL OR PSYCHIATRIC DISORDER: OBSERVATION FOR ANXIETY/ADJUSTMENT DISORDE	20[redacted]
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted] / 1	[redacted] / 42	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1.5 g (gram(s))	BID	Y-M: [redacted]
CITALOPRAM HYDROBROMIDE	20 mg (milligram(s))	QD	Y-M: [redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: [redacted] / -45
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: [redacted] / -44

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1.5 g (gram(s))	BID	Y-M: [redacted]	ONGOING
CITALOPRAM HYDROBROMIDE	20 mg (milligram(s))	QD	Y-M: [redacted]	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: [redacted] / -44	ONGOING
CHLORPROTHIXENE	7.5 mg (milligram(s))	QD	Y-M: [redacted] / 52	ONGOING
ACICLOVIR SODIUM	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
BENZYLPENICILLIN	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
BENZYLPENICILLIN SODIUM	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
CEFOTAXIME SODIUM	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
DEXAMETHASONE SODIUM PHOSPHATE	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
DIAZEPAM	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
KETOPROFEN	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
MANNITOL	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
MIDAZOLAM HYDROCHLORIDE	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
NALBUPHINE HYDROCHLORIDE	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68

			52
OMEPRAZOLE	UNK UNK	OTHER: UNK	Y-M: 20[redacted]-[redacted] / 52 Y-M: 20[redacted]-[redacted] / 68
ONDANSETRON	UNK UNK	OTHER: UNK	Y-M: 20[redacted]-[redacted] / 52 Y-M: 20[redacted]-[redacted] / 68
PARACETAMOL	UNK UNK	OTHER: UNK	Y-M: 20[redacted]-[redacted] / 52 Y-M: 20[redacted]-[redacted] / 68

Event #1: Serious Adverse Event

Event Description	HEADACHES, LOSS OF CONSCIOUSNESS
Preferred term	頭痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 52 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 52): MAGNESIUM: 19.4 [0 - 0] MG/L; [redacted]20[redacted](RX DAY 53): HS TROPONINE I: <5 [0 - 0] NG/L

Microbiology

[redacted]20[redacted] (RX DAY 21): Blood CEREBRAL FLUID CULTURE: -NOT DONE; [redacted]20[redacted] (RX DAY 52): Blood BLOOD CULTURE: -NOT DONE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 52): CHEST RAY: NORMAL; CT CNS: NORMAL; [redacted]20[redacted] (RX DAY 54): MR CNS: NORMAL; [redacted]20[redacted] (RX DAY 57): EEG: NORMAL; [redacted]20[redacted] (RX DAY 68): ECHO: NORMAL; ECG HOLTER: NORMAL

AE Stopped Rx Day	68 (26 DAYS AFTER LAST TREATMENT)
Duration of AE	17 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	HEADACHES, LOSS OF CONSCIOUSNESS
Preferred term	意識消失
AE Onset Date / Rx Day	[redacted]20[redacted] / 52 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 52): MAGNESIUM: 19.4 [0 - 0] MG/L; [redacted]20[redacted] (RX DAY 53): HS TROPONINE I: <5 [0 - 0] NG/L

Microbiology

[redacted]20[redacted] (RX DAY 21): Blood CEREBRAL FLUID CULTURE: -NOT DONE; [redacted]20[redacted] (RX DAY 52): Blood BLOOD CULTURE: -NOT DONE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 52): CHEST RAY: NORMAL; CT CNS: NORMAL; [redacted]20[redacted] (RX DAY 54): MR CNS: NORMAL; [redacted]20[redacted] (RX DAY 57): EEG: NORMAL; [redacted]20[redacted] (RX DAY 68): ECHO: NORMAL; ECG HOLTER: NORMAL

AE Stopped Rx Day	68 (26 DAYS AFTER LAST TREATMENT)
Duration of AE	17 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until

second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の頭痛及び意識消失を発現した。関連する病歴は，脳波異常（5 歳頃），一時的な会話不能状態 5 歳頃），選択的緘黙症及び潰瘍性大腸炎であった。被験者は非アルコール摂取者であった。選択的緘黙症及び不安障害のため，被験者はその他の併用療法として精神科治療を長年受けていた。

20[redacted] 年 [redacted] 月 [redacted] 日，頭痛及び意識消失が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，頭痛及び意識消失は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。

退院時要約による情報を以下に記す：被験者は入院する前日に胸骨後方の胸痛を訴え，胸痛は接触時に悪化した。同様の発作は以前にも認められ，その際には数分間持続した。被験者によると，頭痛，悪心，呼吸困難，視覚障害，並びに左側により顕著な顔面及び腕のしびれ感が認められた。身体的診察中には突発性の会話不能状態が発現し，数秒間持続した。筋緊張の低下も伴っていたが，発作はみられなかった。心拍数は不安のため 130 bpm であり，発作中の血圧は 160/120 mmHg，発作後は 150/100 mmHg であった。その他のすべてのパラメータは正常と判断された。20[redacted] 年 [redacted] 月 [redacted] 日，心臓の診察が再度実施され，新たな所見は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者の母親が被験者の周囲とのコミュニケーションの欠如，食物摂取量の少なさ及び離脱行動に懸念を示したことから，精神科医による診察が行われた。被験者は出血発作を減少させるため，食事量を減らしていた。栄養療法のため，小児胃腸科での治療が継続された。その他の検査結果に異常はみられなかった。当時，主訴の身体的原因を排除した後に精神保健クリニックを受診すること及びおそらく精神科へ紹介することも可能であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は内分泌科の診察を受けた。甲状腺の機能は正常であったが，超音波検査で甲状腺肥大が認められた。心臓学的，神経学的及び内分泌学的診断により，被験者の症状の

最終的な原因を説明することは不可能であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者の状態は改善し，退院した。
治療薬として Dexaven（デキサメタゾン），20%マンニトール，Acix（アシクロビル），Ketonal（ケトプロフェン），Midanium（ミダゾラム），Nalpain，Ondansetron accord（オンダンセトロン塩酸塩水和物），Biotaksym（セフォタキシムナトリウム），Penicillinum crystallisatum, Polprazol（オメプラゾール），Relanium（ジアゼパム），Tarcefoksym（セフォタキシムナトリウム），アザチオプリン，Chlorprothixen，5%ブドウ糖，Kabipac，0.9%塩化ナトリウム，Nutridrink，Paracetamol b. braun（アセトアミノフェン），Paracetamol kabi（アセトアミノフェン），ペニシリン及びアセトアミノフェンが投与された。

The patient's past medications include:

VALPROIC ACID for LOSS OF CONTACT (20[redacted] - 20[redacted])

Causality for HUMIRA (Blinded)

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1) Loss of consciousness (10024855) (Loss of consciousness (10024855)) [v.20.1] [10024855]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Headache (10019211) (Headache (10019211)) [v.20.1] [10019211]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of HEADACHES, LOSS OF CONSCIOUSNESS

- Investigator: N/A

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ANA SCREENING TEST: Negative

[redacted] 20[redacted] ANTI-NEURON CELL SURFACE ANTIGEN ANTIBODIES: None

[redacted] 20[redacted] APTT: 20.2 No Unit

[redacted] 20[redacted] APTT: 26.0 No Unit

[redacted] 20[redacted] BASOPHIL: 0.02 X10**3/MCL

[redacted] 20[redacted] BASOPHIL: 0.01 X10**3/MCL

[redacted] 20[redacted] BASOPHIL PERCENTAGE: 0.3 %

[redacted] 20[redacted] BASOPHIL PERCENTAGE: 1 %

[redacted] 20[redacted] BLOOD CULTURE: NEGATIVE

[redacted] 20[redacted] BLOOD PRESSURE (AFTER LOSS OF CONTACT): 150/100 mmHG

[redacted] 20[redacted] BLOOD PRESSURE (DURING LOSS OF CONTACT): 160/120 mmHG

[redacted] 20[redacted] BLOOD-VENOUS-AEROBIC BACTERIA: Negative

[redacted] 20[redacted] BNP: 19.9 PG/ML

[redacted] 20[redacted] BODY WEIGHT: 43 KG

[redacted] 20[redacted] BODY WEIGHT: 43 KG

[redacted] 20[redacted] BODY WEIGHT: 43 KG

[redacted] 20[redacted] CALCIUM: 2.47 MMOL/L

[redacted] 20[redacted] CEREBRAL FLUID CULTURE: NEGATIVE

[redacted] 20[redacted] CEREBROSPINAL FLUID (CSF) ANALYSIS: Appearance l(CSF): colourless, clear, Appearance 2 (CSF): colourless, clear;

[redacted] 20[redacted] CERVICAL SPINE X-RAY (AP AND LATERAL VIEW): Radiologically normal image.

[redacted] 20[redacted] CHEST X-RAY: NORMAL; Lung fields without any focal lesions. No fluid in the pleural cavity. Normal cardiac silhouette. Artifacts in the supraclavicular area on the left.

[redacted] 20[redacted] CK: 36.0 U/L

[redacted] 20[redacted] CREATININE: 0.46 mg/dL

[redacted] 20[redacted] CRP: 0.2 mg/dL

[redacted] 20[redacted] CT SCAN WITHOUT CONTRAST: NORMAL

[redacted] 20[redacted] D-DIMER: 2.84 mg/dL

[redacted] 20[redacted] D-DIMER: 0.79 MG/L

Unknown date ECG (SCREENING): Normal

[redacted] 20[redacted] ECG HOLTER: CONCLUSIONS: Recording appropriate for the age of the patient.

[redacted] 20[redacted] ECHOCARDIOGRAM: CONCLUSION: Normal echocardiogram.

[redacted] 20[redacted] EEG: CONCLUSIONS: Recording of the brain bioelectrical activity when awake is borderline normal.

[redacted] 20[redacted] EEG WITH VISUAL PROVOCATION: CONCLUSIONS: Recording of the brain bioelectrical activity when awake is borderline normal.

[redacted] 20[redacted] ELECTROCARDIOGRAM: Normal

[redacted] 20[redacted] EOSINOPHIL: 0.02 X10**3/MCL

[redacted] 20[redacted] EOSINOPHIL PERCENTAGE: 0.3 %

[redacted] 20[redacted] EOSINOPHIL PERCENTAGE: 0.3 %

[redacted] 20[redacted] ERYTHROCYTES (CSF): 1 MCL

[redacted] 20[redacted] FE: 28 MCG/DL

[redacted] 20[redacted] GLUCOSE: 118 mg/dL

[redacted] 20[redacted] GLUCOSE: 119 mg/dL

[redacted] 20[redacted] GLUCOSE (CSF): 58 mg/dL

[redacted] 20[redacted] HCT: 35.2 %

[redacted] 20[redacted] HCT: 32.3 %

[redacted] 20[redacted] HCT: 33.5 %

[redacted] 20[redacted] HCT: 33.6 %

[redacted] 20[redacted] HEART RATE: 130 BPM

[redacted] 20[redacted] HEMOGLOBIN: 11 G/DL

[redacted] 20[redacted] HGB: 11.0 G/DL

[redacted] 20[redacted] HGB: 10.8 G/DL

[redacted] 20[redacted] HGB: 10.4 G/DL

[redacted] 20[redacted] HGB: 10.9 G/DL

[redacted] 20[redacted] INR: 1.09 No Unit

[redacted] 20[redacted] INR: 1.14 No Unit

[redacted] 20[redacted] IONIZED CALCIUM: 1.09 MMOL/L

[redacted] 20[redacted] LEUCOCYTES (CSF): 1 MCL

[redacted] 20[redacted] LYMPHOCYTE: 1.25 X10**3/MCL

[redacted] 20[redacted] LYMPHOCYTE: 20.7 %

[redacted] 20[redacted] LYMPHOCYTE: 1.45 X10**3/MCL

[redacted] 20[redacted] LYMPHOCYTE PERCENTAGE: 18.9 %

[redacted] 20[redacted] MAGNESIUM: 19.4 MG/L

[redacted] 20[redacted] MCH: 30.6 PG

[redacted] 20[redacted] MCH: 30.6 PG

[redacted] 20[redacted] MCH: 30.9 PG

[redacted] 20[redacted] MCH: 30.2 PG

[redacted] 20[redacted] MCHC: 31.3 G/DL

[redacted] 20[redacted] MCHC: 33.4 G/DL

[redacted] 20[redacted] MCHC: 31 .0 G/DL

[redacted] 20[redacted] MCHC: 32.4 G/DL

[redacted] 20[redacted] MCV: 98.1 FL

[redacted] 20[redacted] MCV: 91.5 FL

[redacted] 20[redacted] MCV: 99.4 FL

[redacted] 20[redacted] MCV: 93.1 FL

[redacted] 20[redacted] MENINGITIS PANEL: Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenza (CSF): negative

[redacted] 20[redacted] MENINGITIS PANEL 9: CMV, EBY, adenovirus, HSY type 1 and 2, VZV, enterovirus, parechovirus, HHV type 6 and 7, parvovirus B19 (CSF): negative;

[redacted] 20[redacted] MONOCYTE: 0.50 X10**3/MCL

[redacted] 20[redacted] MONOCYTE: 8.1 %

[redacted] 20[redacted] MONOCYTE: 0.57 X10**3/MCL

[redacted] 20[redacted] MONOCYTE PERCENTAGE: 7.6 %

[redacted] 20[redacted] MPV: 10.40 FL

[redacted] 20[redacted] MPV: 10.5 FL

[redacted] 20[redacted] MPV: 9.90 FL

[redacted] 20[redacted] MPV: 10.2 FL

[redacted] 20[redacted] MRI: CNS-NORMAL

[redacted] 20[redacted] NEUTROPHIL: 72.9 %

[redacted] 20[redacted] NEUTROPHIL: 4.82 X10**3/MCL

[redacted] 20[redacted] NEUTROPHIL: 4.97 X10**3/MCL

[redacted] 20[redacted] NEUTROPHIL PERCENTAGE: 70.8 %

[redacted] 20[redacted] PDW: 10.2 FL

[redacted] 20[redacted] PLATELET COUNT: 431 X10**3/MCL

[redacted] 20[redacted] PLT: 460 X10**3/MCL

[redacted] 20[redacted] PLT: 368 X10**3/MCL

[redacted] 20[redacted] PLT: 371 X10**3/MCL

[redacted] 20[redacted] POTASSIUM: 3.54 MMOL/L

[redacted] 20[redacted] PROTEIN: 6.63 G/DL

[redacted] 20[redacted] PROTEIN (CSF): 34 mg/dL

[redacted] 20[redacted] PT: 12.0 No Unit

[redacted] 20[redacted] PT: 12.5 No Unit

[redacted] 20[redacted] RBC: 3.59 X10**6/MCL

[redacted] 20[redacted] RBC: 3.53 X10**6/MCL

[redacted] 20[redacted] RBC: 3.37 X10**6/MCL

[redacted] 20[redacted] RBC: 3.61 X10**6/MCL

[redacted] 20[redacted] RDW-CV: 16.5 %

[redacted] 20[redacted] RDW-CV: 16.2 %

[redacted] 20[redacted] RDW-CV: 15.9 %

[redacted] 20[redacted] RDW-SD: 56.6 FL

[redacted] 20[redacted] RDW-SD: 50.5 FL

[redacted] 20[redacted] SERUM ALT: 10 IU/L

[redacted] 20[redacted] SERUM AST: 27 IU/L

[redacted] 20[redacted] SERUM CA: 2.47 MMOL/L

[redacted] 20[redacted] SERUM CA: 2.33 MMOL/L

[redacted] 20[redacted] SERUM CREATININE: 0.46 mg/dL

[redacted] 20[redacted] SERUM GLUCOSE: 90 mg/dL

[redacted] 20[redacted] SERUM K: 3.54 MMOL/L

[redacted] 20[redacted] SERUM MG: 19.1 MG/L

[redacted] 20[redacted] SERUM NA: 139 MMOL/L

[redacted] 20[redacted] SERUM UREA: 24 mg/dL

[redacted] 20[redacted] SGOT/AST: 27 IU/L

[redacted] 20[redacted] SGPT/ALT: 10 IU/L

[redacted] 20[redacted] SODIUM: 139 MMOL/L

[redacted] 20[redacted] TIBC: 317 MCG/DL

[redacted] 20[redacted] TOTAL PROTEIN: 7.04 G/DL

[redacted] 20[redacted] TROPONIN I: <5 NG/L

[redacted] 20[redacted] TSH U: 0.431 IU/mL

Unknown date ULTRASOUND OF THYROID (DURING HOSPITALIZATION): Enlarged thyroid, slightly hypoechoic, mostly peripherally, heterogenic, no focal lesions. Right lobe: 17.1 x 17.5 mm Left lobe: 15.9 x 14.4

[redacted] 20[redacted] URIC ACID: 24 mg/dL

[redacted] 20[redacted] WBC: 6.64 X10**3/MCL

[redacted] 20[redacted] WBC: 6.61 X10**3/MCL

[redacted] 20[redacted] WBC: 6.62 X10**3/MCL

[redacted] 20[redacted] WBC: 7.02 X10**3/MCL

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD	1[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: CAMPYLOBACTER INFECTION	20[redacted]
OTHER: CLOSTRIDIUM DIFF. INFECTION	20[redacted]
Ulcerative colitis	20[redacted]
ANEMIA: ANEMIA	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 15	28

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -138
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -99
FERRIC HYDROXIDE POLYMALTOSE COMPLEX	1 DF (dosage form)	QD	Y-M: 20[redacted] / -32
DICLOFENAC POTASSIUM	1 TABLET	QD	Y-M: 20[redacted] / -28
LEKOVIT CA	1 TABLET	QD	Y-M: 20[redacted] / -28
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -28

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -138	Y-M: 20[redacted] / 29
FERRIC HYDROXIDE POLYMALTOSE COMPLEX	1 DF (dosage form)	QD	Y-M: 20[redacted] / -32	Y-M: 20[redacted] / 15
DICLOFENAC POTASSIUM	1 TABLET	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / 18
LEKOVIT CA	1 TABLET	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / 18
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / 24
AKRITOIN	100 mg (milligram(s))	TID	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 7
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 8	Y-M: 20[redacted] / 18
FERROUS TARTRATE	1 DF (dosage form)	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 18
BLOOD AND RELATED PRODUCTS	2 DF (dosage form)	QD	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
DEXTROSE AND SODIUM CHLORIDE INJECTION	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
PARACETAMOL	1 g (gram(s))	QD	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
CEFTAZIDIME	2 g (gram(s))	TID	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 29
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 21
CALCIUM	10 mL (millilitre(s))	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] /

			20	91
DEXTROSE AND SODIUM CHLORIDE INJECTION	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 23
BLOOD AND RELATED PRODUCTS	2 DF (dosage form)	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
HYDROCORTISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
IBUPROFEN	400 mg (milligram(s))	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
PARACETAMOL	1 g (gram(s))	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 29
HYDROCORTISONE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 24
OSMOTAN	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 27
POTASSIUM CHLORIDE	1 TABLET	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 29
HYDROCORTISONE	50 mg (milligram(s))	TID	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 29
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted] / 30	ONGOING
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / 30	ONGOING
PREDNISONE	20+10 mg (milligram(s))	BID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 50
FERROUS TARTRATE	1 DF (dosage form)	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 91
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 91
POTASSIUM CHLORIDE	1 TABLET	BID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 91
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 60
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 70
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 80
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 91

Event #1: Serious Adverse Event

Event Description	WORSENING OF ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 18 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	

[redacted]20[redacted] (RX DAY 19): BLOOD TRANSFUSION: ANEMIA PARTIALLY RESOLVED. NO ADVERSE EVENTS WERE OBSERVED DURING AND AFTER TRANSFUSION.; [redacted]20[redacted] (RX DAY 21): ECG: SINUS RHYTHM 100 PER MINUTE, PR INTERVAL, QTC, QTC COMPLEX, ARE NORMAL, T - WAVES ARE FLAT (NO DEPRESSIONS, NO INVERSIONS, NO ELEVATIONS)

AE Stopped Rx Day	91 (76 DAYS AFTER LAST TREATMENT)
Duration of AE	74 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INTESTINAL BLEEDING
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 19 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	31 (16 DAYS AFTER LAST TREATMENT)
Duration of AE	13 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE

Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

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

Event Description	PERICARDITIS
Preferred term	心膜炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 21 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	29 (14 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and
Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum
dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching
placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg
(maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.

MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の心膜炎及び貧血の悪化が認められた。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。

本試験では，最初の 8 週間はすべての被験者がアダリムマブの投与を受けることとしていたが，当該被験者は投与 2 週時まで盲検下でアダリムマブの投与を受けた。

20[redacted] 年 [redacted] 月 [redacted] 日のスクリーニング時に貧血が認められた（臨床検査値は報告されず）。

20[redacted] 年 [redacted] 月 [redacted] 日，貧血の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，心膜炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，心膜炎は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血の悪化は回復した。

咽喉痛，貧血及び C 反応性たん白濃度の著しい上昇の徴候及び症状がみられた。C 反応性たん白高値は当初 20[redacted] 年 [redacted] 月 [redacted] 日のベースライン時に認められていた。

20[redacted] 年 [redacted] 月 [redacted] 日，臨床検査の結果，ヘモグロビン低値及び C 反応性たん白高値の持続がみられた。治験責任医師は，被験者の両親に連絡を取り，輸血，並びに感染原因及び感染源の評価

のため被験者を入院させることを提案した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 1 日，被験者は心膜炎と診断された。

胸痛，頻脈，全身倦怠及び C 反応性たん白濃度高値が認められた。心エコー検査により心膜炎と診断され（心嚢液），静脈内ステロイド及びセフタジジムの経験的投与が行われた。心膜炎の正確な原因は不明であったが，一つの可能性としてアダリムマブの副作用が挙げられた。血清学的検査の結果はすべて陰性であった。心膜炎は，静脈内ステロイド療法の開始後に迅速に回復した。貧血は，血液 4 単位の輸血後にある程度回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

本事象に関連したリスク因子には，潰瘍性大腸炎及びアダリムマブ投与があった。

治療薬として Ferroplex，オメプラゾール，アザチオプリン，ヒドロコルチゾン，Kalipoz，イブプロフェン，Encorton，アセトアミノフェン及びブドウ糖／塩化ナトリウムが投与され，輸血が行われた。

Causality for HUMIRA (Open Label)

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1) Pericarditis (10034484) (Pericarditis (10034484)) [v.21.0] [10034484]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Yes

2) Anemia aggravated (10054309) (Anaemia (10002034)) [v.21.0] [10054309]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Alternative Etiology for HUMIRA (Open Label)

Event of PERICARDITIS

- Investigator: N/A

- AbbVie: N/A

Event of WORSENING OF ANEMIA

- Investigator: Intestinal bleeding

- AbbVie: A common complication of UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CRP: Elevated, 200 mg/dl

[redacted] 20[redacted] ECG: RMZ 100 / MIN, Q, QTC, QRS - IN NORM THREATS T PLAYED

[redacted] 20[redacted] Electrocardiogram: Not clinical significant-abnormal T waves

[redacted] 20[redacted] Hemoglobin: 6.0 G/DL (normal 11.0 to 14.3)

[redacted] 20[redacted] HEMOGLOBIN: 9.2 G/DL (normal 11.0 to 14.3)

[redacted] 20[redacted] High-sensitivity C-reactive protein: 196.8 MG/L (normal 0 to 5)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
手首関節骨折	X			

Treatment Group	Age at Study Start	Sex	Race
IHD-MHD	[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: HB 7.3G/DL	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: POSITIVE QUANTIFERON TEST	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	55
MHD	[redacted]20[redacted] / 56	[redacted]20[redacted] / 357	309

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -220
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -161
CALCIUM	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14
COLECALCIFEROL	2 gtt (drop(s))	QD	Y-M: 20[redacted] / -14
ISONIAZID	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
POTASSIUM	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
SUCCIFER	5 mL (millilitre(s))	BID	Y-M: 20[redacted] / -14
VIGRAN	1 TABLET	QD	Y-M: 20[redacted] / -14

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -220	ONGOING
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -161	Y-M: 20[redacted] / 127
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 29
CALCIUM	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 36
COLECALCIFEROL	2 gtt (drop(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 36
POTASSIUM	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 36
SUCCIFER	5 mL (millilitre(s))	BID	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 73
ISONIAZID	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 127
VIGRAN	1 TABLET	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 127
PARACETAMOL	200 mg (milligram(s))	QD	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 10

Event #1: Serious Adverse Event

Event Description	WRIST FRACTURE LEFT
Preferred term	手首関節骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 10
Age at AE Onset	[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 10): X-RAY: HAND WRIST FRACTURE LEFT; PLASTER DRESSING: PLASTER WAS REMOVED ON [redacted]20[redacted].	
AE Stopped Rx Day	29
Duration of AE	20 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MECHANICAL INJURY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	PERSIST OR SIGNIF DISABILITY/INCAPACITY, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and
Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum
dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching
placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg
(maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit

and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，[redacted] 歳の男児（ポーランド）であり，重篤な有害事象の左手首関節骨折を発現した。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，左手首関節骨折が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左手首関節骨折は回復した。

被験者は階段から転落した。手の X 線検査の結果，手根骨骨折が認められ，ドレッシングプラスターによる固定が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，プラスターを除去した。

治療薬としてアセトアミノフェンが投与された。

Causality for HUMIRA (Blinded)

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1) Wrist fracture (10048049) (Wrist fracture (10048049)) [v.21.0] [10048049]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of WRIST FRACTURE LEFT

- Investigator: Mechanical injury.

- AbbVie: A Trauma.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] X-RAY: Hand wrist fracture left.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]
OTHER: NAUSEA AND VOMITING WHEN PATIENT GOES TO TOILET	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -168
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -82
HYDROCORTISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -33
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / -17

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / -17	Y-M: 20[redacted] / 28
METHYLPREDNISOLONE	8 mg (milligram(s))	QD	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 35
METHYLPREDNISOLONE	6 mg (milligram(s))	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 42
METHYLPREDNISOLONE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 49
METHYLPREDNISOLONE	2 mg (milligram(s))	QD	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 57
ADALIMUMAB	40 mg (milligram(s))	OTHER: EVERY WEEK	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 111
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 71
METHYLPREDNISOLONE	24 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 111
NADROPARIN CALCIUM	5700 IU (international unit(s))	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 177
ALPRAZOLAM	0.5 mg (milligram(s))	BID	Y-M: 20[redacted] / 111	Y-M: 20[redacted] / 113
CEFUROXIME	1.5 g (gram(s))	BID	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 113
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 113
NAPROXEN	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 115

ALIZAPRIDE	50 mg (milligram(s))	QID	Y-M: 20[redacted] / Y-M: 20[redacted] / 112 122
NADROPARIN CALCIUM	2850 IU (international unit(s))	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 112 122
RANITIDINE HYDROCHLORIDE	50 mg (milligram(s))	TID	Y-M: 20[redacted] / Y-M: 20[redacted] / 112 130
TRAMADOL HYDROCHLORIDE	50 mg (milligram(s))	QID	Y-M: 20[redacted] / Y-M: 20[redacted] / 115 122

Event #1: Serious Adverse Event

Event Description	WORSENING ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 38
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 112): TOTAL COLOPROCTECTOMY BY SINGLE INCISION LAPAROSCOPIC: REMISSION OF ULCERATIVE COLITIS

AE Stopped Rx Day	274 (232 DAYS AFTER LAST TREATMENT)
Duration of AE	237 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	STUDY DISEASE RELATED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and
Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum
dose of 40 mg) at Week 4 and Week 6.

ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女性（ベルギー）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（汎大腸炎）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。薬剤投与により潰瘍性大腸炎の症状（排便回数増加及び血便）に改善が認められなかったことから，手術が予定された。20[redacted] 年 [redacted] 月 [redacted] 日，単孔式腹腔鏡下手術により結腸直腸全摘除が行われた。腹壁の術後（静脈）血栓症が認められ，

Fraxiparin（ヘパリンカルシウム）が投与された。術後の悪心及び嘔吐はコルチコイドの投与により回復した。潰瘍性大腸炎は寛解となった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬としてラニチジン，Fraxiparine（ヘパリンカルシウム），Xanax（アルプラゾラム），Litican，Motilum（ドンペリドン），Dipidolor，アセトアミノフェン，Dafalgan（アセトアミノフェン），Tradonal（トラマドール塩酸塩），Zantac（ラニチジン塩酸塩），Taradyl，Naprosyne（ナプロキセン），Zinacef（セフロキシム），メトロニダゾール，Primperan（メトクロプラミド），Catapressan（クロニジン塩酸塩），オンダンセトロン，Solu-medrol（メチルプレドニゾロンコハク酸エステルナトリウム）及び Solu-cortef（ヒドロコルチゾンコハク酸エステルナトリウム）が投与された。

The patient's past medications include:

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

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

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

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

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING ULCERATIVE COLITIS

- Investigator: Study disease related

- AbbVie: The underlying UC

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Colonoscopy: Rectum, sigmoid, Descending/Transverse colon - 3 (Severe disease - spontaneous bleeding, ulceration). Ascending colon/cecum (Moderated disease - marked erythema, absent vascular pattern, friability, erosions).

Subject [redacted](Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD-MSD-FNREIND	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: IBD	20[redacted]
Ulcerative colitis	20[redacted]
OSTEOPENIA: BONE DENSITY DECREASE (DENSITOMETRY)	20[redacted]
ANEMIA: SIDEROPENIC	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 45	58
MSD	[redacted]20[redacted] / 60	[redacted]20[redacted] / 262	214
FNREIND	[redacted]20[redacted] / 274	[redacted]20[redacted] / 360	94

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -290
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -290
ESCHERICHIA COLI	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -245
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -245
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -245
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -121
CITRIC ACID	18.0 g (gram(s))	BID	Y-M: 20[redacted] / -40
MAGNESIUM OXIDUM LEVE	3.5 g (gram(s))	BID	Y-M: 20[redacted] / -40
SODIUM PICOSULFATE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -40

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
ESCHERICHIA COLI	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -245	ONGOING
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -245	ONGOING
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -245	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -121	ONGOING
PARACETAMOL	250 mg (milligram(s))	OTHER: [redacted].20[redacted] 250 MG [redacted].20[redacted] 500 MG [redacted].20[redacted] 250 MG	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 336
HYLAK	40 gtt (drop(s))	OTHER: [redacted].20[redacted] [redacted].20[redacted]	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 223
PARACETAMOL	400 mg (milligram(s))	QID	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 238
CIPROFLOXACIN HYDROCHLORIDE	200 mg (milligram(s))	BID	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 243
METRONIDAZOLE	430 mg (milligram(s))	TID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 242
PREDNISONE	15 mg (milligram(s))	BID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 256
OMEPRAZOLE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 270
CIPROFLOXACIN	250 mg (milligram(s))	BID	Y-M: 20[redacted]	Y-M: 20[redacted]

HYDROCHLORIDE			[redacted] / 243 / 248
METRONIDAZOLE	250 mg (milligram(s))	BID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 243 / 248
FLUCONAZOLE	100 mg (milligram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 243 / 270
PREDNISONE	12.5 mg (milligram(s))	BID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 257 / 261
METHYLPREDNISOLONE SODIUM SUCCINATE	250 mg (milligram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 262 / 262
METHYLPREDNISOLONE SODIUM SUCCINATE	40 mg (milligram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 263 / 264
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 265 / 297
CITRIC ACID	18 g (gram(s))	BID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 269 / 269
MAGNESIUM OXIDUM LEVE	3.5 g (gram(s))	BID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 269 / 269
SODIUM PICOSULFATE	10 mg (milligram(s))	BID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 269 / 269

Event #1: Serious Adverse Event

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 235
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 235): Blood BLOOD CULTURE:; Other SWAB SWAB FROM THE TONSILS: POSITIVE-STREPTOCOCCUS VIRIDANS HAEMOPHILUS PARAINFLUENZAE; Other SWAB NASAL SWAB:; Other STOOL RECTAL SWAB: POSITIVE-ENTEROCOCCUS SPECIES; Urine AEROBIC CULTIVATION:

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 235): CHEST X-RAY: NO PATHOLOGICAL CHANGES

AE Stopped Rx Day	243
Duration of AE	9 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COLITIS ULCEROSA FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 269
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted](RX DAY 238): S_FERI: 531.24 [15 - 150] MCG/ML; [redacted]20[redacted] (RX DAY 269): FE_S: 4.9 [9 - 21.5] MCMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 269): Other SWAB FROM THE TONSILS SWAB FROM THE TONSILS: POSITIVE-ENTEROBACTER CLOACAE GROUP ++

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 270): RECTOSIGMOIDOSKOPY: UC, MAYO ENDOSCOPIC SCORE 3

AE Stopped Rx Day	277
Duration of AE	9 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until

second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（スロバキア共和国）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な有害事象の急性鼻咽喉炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，発熱，疲労，体重減少，腹痛及び血便の徴候及び症状のため入院し，薬剤が投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬としてメトロニダゾール，Entizol（メトロニダゾール），Diflucan（フルコナゾール），prednisone，Helicid（オメプラゾール），Ciprinol（シプロフロキサシン塩酸塩水和物），Perfalgan（アセトアミノフェン）及び Medociprin（シプロフロキサシン塩酸塩水和物）が投与された。

The patient's past medications include:

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

Causality for HUMIRA (Blinded)

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1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.18.0] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of UC FLARE

- Investigator: Colitis ulcerosa flare

- AbbVie: The underlying disorder UC

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] hemoglobin: 108 G/L (normal 110 to 150)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（スロバキア共和国）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，コルチコステロイド抵抗性の潰瘍性大腸炎再燃の徴候が持続していたため，被験者は入院した。潰瘍性大腸炎の再燃に伴う徴候及び症状として，発熱，体重減少，血便，頻回の排便及び炎症活性の増強が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として prednisone が投与された。

The patient'spast medications include:

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

HYLAK for DIARRHEA ([redacted] 20[redacted] - [redacted] 20[redacted])

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

SOLUMEDROL for ULCERATIVE COLITIS FLARE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.19.1] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Alternative Etiology for HUMIRA (Open Label)

Event of UC FLARE

- Investigator: ULCERATIVE COLITIS.

- AbbVie: THE UNDERLYING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] RBC: 3.39 X10**12/L (normal 3.80 to 5.20)

[redacted] 20[redacted] FE-S: 531.24 MCG/ML (normal 15 to 150.0)

[redacted] 20[redacted] C-reactive protein: 56.1 MG/L (normal 0 to 5)

[redacted] 20[redacted] FE-S: 4.9 MCMOL/L (normal 9.0 to 21.5)

[redacted] 20[redacted] WBC: 3.30 X10**9/L (normal 4.00 to 12.00)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD-MHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
Ulcerative colitis	20[redacted]
SCOLIOSIS: ADOLESCENT IDIOPATHIC SCOLIOSIS	20[redacted]
ANEMIA: SIDEROPENIC	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MHD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	310

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -254
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -254
OMEPRAZOLE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / -103
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -103
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -70
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -70
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -70
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -40
CITRIC ACID	18.0 g (gram(s))	BID	Y-M: 20[redacted] / -21
MAGNESIUM OXIDUM LEVE	3.5 g (gram(s))	BID	Y-M: 20[redacted] / -21
SODIUM PICOSULFATE	10.0 mg (milligram(s))	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
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -254	ONGOING
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -70	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -40	ONGOING
PARACETAMOL	500 mg (milligram(s))	OTHER: [redacted] 06-	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 211
PARACETAMOL	630 mg (milligram(s))	QID	Y-M: 20[redacted] / 190	Y-M: 20[redacted] / 192
AUGMENTIN	1.2 g (gram(s))	TID	Y-M: 20[redacted] / 190	Y-M: 20[redacted] / 195
AUGMENTIN	375 mg (milligram(s))	TID	Y-M: 20[redacted] / 195	Y-M: 20[redacted] / 201

Event #1: Serious Adverse Event

Event Description	PHARYNGITIS ACUTA
Preferred term	咽頭炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 190
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 191): Other NASAL SWAB AEROBIC CULTIVATION:; Stool AEROBIC CULTIVATION:; Other SWAB FROM THE TONSILS AEROBIC CULTIVATION: POSITIVE-STREPTOCOCCUS ANGINOSUS +; Urine AEROBIC CULTIVATION:

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 190): ULTRASOUND EXAMINATION: WITHOUT PATHOLOGICAL FINDINGS

AE Stopped Rx Day	195
Duration of AE	6 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until

second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女性（スロバキア共和国）であり，重篤な有害事象の急性咽頭炎を発現した。関連する病歴は，潰瘍性大腸炎，潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎）及び鉄欠乏性貧血であった。

20[redacted] 年 [redacted] 月 [redacted] 日，急性咽頭炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性咽頭炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，体の痛み，全身脱力，最高体温 39°C，乾性咳嗽，咽喉痛，食欲減退及び打診音の異常が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，診断及び治療のため，被験者は救急病院に入院した。入院時，気道感染及び脱水の臨床徴候がみられたが，神経学的所見は正常であった。治療として Augmentin（アモキシシリン／クラブラン酸）及び Perfalgan（アセトアミノフェン）の投与，非経口的水分補給，並びに対症療法が開始された。入院当初は発熱が認められたがその後解熱し，排便は 1 日 1 回，食事に耐性もみられ，問題はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師によると，被験者には本事象に関連したリスク因子はなかった。

治療薬として Perfalgan（アセトアミノフェン）及び Augmentin（アモキシシリン／クラブラン酸）が投与された。

The patient's past medications include:

OMEPRAZOL for COMBINED TREATMENT WITH PREDNISON ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISON for DISEASE ACTIVATION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1)　Acute pharyngitis (10001002)　(Pharyngitis (10034835))　[v.20.0]　[10001002]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of PHARYNGITIS ACUTE

- Investigator: Ulcerative colitis

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Hemoglobin: 125 G/L (normal 120 to 155)

[redacted] 20[redacted] Nasal swab (aerobic cultivation): Negative

[redacted] 20[redacted] STOOL (aerobic cultivation): Negative

[redacted] 20[redacted] Swab from the tonsils (Aerobic cultivation): Positive(streptococcus anginosus)

[redacted] 20[redacted] Ultrasound examination: Without pathological findings

[redacted] 20[redacted] Urine (aerobic cultivation): Negative

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD-MHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MHD	[redacted]20[redacted] / 60	[redacted]20[redacted] / 120	74

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -120

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 68
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 64
NUTRIENTS NOS	200 mcL (microlitre(s))	BID	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 64
ONDANSETRON	50 mg (milligram(s))	PRN	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 64

Event #1: Serious Adverse Event

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 52
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 59): CRP: 49 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 59): Stool STOOL MICROBIOLOGY: -NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 72): SIGMOIDESCOPY: SICK COLON MUCOSA SARTING DEPTH OF 30 CM. POSITIVE COLON COLITIS/BLEEDING.

AE Stopped Rx Day	64
Duration of AE	13 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DISEASE FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,

MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女性（イスラエル）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，潰瘍性大腸炎（左側）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な有害事象の発熱が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な有害事象の体重減少が発現し，持続していた。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，下痢が発現し，治験薬の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，疾患の再燃のため被験者は入院し，発熱及び下痢の持続と共に，非重篤な有害事象の疲労，悪心及び嘔吐の症状が認められた。併用薬が投与された。20[redacted] 年 [redacted] 月 [redacted] 日，治験薬の投与が再開されたが，非反応であったため，投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，悪心，嘔吐及び疲労は回復し，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，発熱は回復した。

治療薬としてアセトアミノフェン，Zofran（オンダンセトロン塩酸塩水和物），Peptamen 及び Flagyl（メトロニダゾール）が投与された。

The patient's past medications include:

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

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

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.21.0] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of UC FLARE

- Investigator: Disease flare.

- AbbVie: The underlying disorder Ulcerative Colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CRP: 49 MG/L (normal 0 to 5)

[redacted] 20[redacted] SIGMOIDOSCOPY: Sick colon mucosa starting depth of 30 cm. Positive colon colitis/bleeding.

[redacted] 20[redacted] STOOL MICROBIOLOGY: Negative

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHDOL-MHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: MALNUTRITION	NOT REPORTED
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHDOL	[redacted]0[redacted] / 1	[redacted]20[redacted] / 43	56
MHD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 267	224

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -129
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -127
AZATHIOPRINE	75 mg (milligram(s))	QD	Y-M: 20[redacted] / -47
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -47
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -47
IMIPENEM	500 mg (milligram(s))	QID	Y-M: 20[redacted] / -40
METRONIDAZOLE	250 mg (milligram(s))	TID	Y-M: 20[redacted] / -40

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -127	ONGOING
AZATHIOPRINE	75 mg (milligram(s))	QD	Y-M: 20[redacted] / -47	ONGOING
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 50
CEFUROXIME	750 mg (milligram(s))	TID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 71
SACCHAROMYCES BOULARDII	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 76
IBUPROFEN	200 mg (milligram(s))	QD	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 69
PARACETAMOL	500 mg (milligram(s))	OTHER: WHEN NEEDED	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 71
AMIKACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 75
BUDESONIDE	500 mcg (microgram(s))	BID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 76
ENOXAPARIN SODIUM	33 mg (milligram(s))	QD	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 78
CEFTRIAXONE SODIUM	2 g (gram(s))	BID	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 78
HYDROXYZINE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 78
CLEMASTINE FUMARATE	1 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 79
NAPROXEN	125 mg (milligram(s))	BID	Y-M: 20[redacted] /	Y-M: 20[redacted] / 79

			71
ALBUMIN HUMAN	50 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 73 Y-M: 20[redacted]-[redacted] / 77
PHYTOMENADIONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 74 Y-M: 20[redacted]-[redacted] / 75

Event #1: Serious Adverse Event

Event Description	ERYTHREMA NODOSUM
Preferred term	結節性紅斑
AE Onset Date / Rx Day	[redacted]20[redacted] / 65
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	79
Duration of AE	15 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ERYTHEMA NODOSUM MIGHT HAVE OCCURRED DUE TO URINARY TRACT INFECTION IN PERSON WITH CU
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	URINAL TRACT INFECTION
Preferred term	尿路感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 65
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	72

Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THAT WAS URINARY TRACT INFECTION, THERE WAS NO CAUSE FOUND.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.

3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:09:56
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の尿路感染及び結節性紅斑を発現した。
20[redacted] 年 [redacted] 月 [redacted] 日，尿路感染及び結節性紅斑が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，尿路感染は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，結節性紅斑は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は尿路感染の疑いのため入院した。身体的診察において，両下肢に結節性紅斑が認められた。排尿時の不快感及び両下肢の結節性紅斑を含む徴候及び症状がみられ，抗生剤が投与された。
治療薬として，Zinacef（セフロキシム），Nurofen（イブプロフェン），アセトアミノフェン，アミカシン，Clexane（エノキサパリンナトリウム），ヒドロキシジン，Biotraxon（セフトリアキソンナトリウム水和物），ナプロキセン，20%アルブミン，Clemastin（クレマスチンフマル酸塩），Enterol 及び Zinnat（セフロキシム　アキセチル）が投与された。

The patient's past medications include:

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

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

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

Causality for HUMIRA (Blinded)

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1)　Urinary tract infection (10046571)　(Urinary tract infection (10046571))　[v.22.0]　[10046571]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

2) Erythema nodosum (10015226) (Erythema nodosum (10015226)) [v.22.0] [10015226]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of URINAL TRACT INFECTION

- Investigator: THAT WAS URINARY TRACT INFECTION, THERE WAS NO CAUSE FOUND.

- AbbVie: Not Applicable.

Event of ERYTHREMA NODOSUM

- Investigator: ERYTHEMA NODOSUM MIGHT HAVE OCCURRED DUE TO URINARY TRACT INFECTION IN PERSON WITH UC.

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
感染性腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
IHD-MSD-FREIND	1[redacted]	MALE	ASIAN

Medical History	Onset Year
MIGRAINE HEADACHE: MIGRAINE HEADACHE	NOT REPORTED
OTHER: ACNE VULGARIS	NOT REPORTED
OTHER: CHRONIC RHINITIS	NOT REPORTED
OTHER: DIARRHEA	NOT REPORTED
OTHER: RIGHT COXITIS	NOT REPORTED
Ulcerative colitis	20[redacted]
OTHER: UPPER RESPIRATORY TRACT INFECTION	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted] / 1	[redacted] / 43	56
MSD	[redacted] / 57	[redacted] / 113	63
FREIND	[redacted] / 120	[redacted] / 197	87
2nd FLARE OL ADA	[redacted] / 207	[redacted] / 355	158

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -338
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -253
CLOSTRIDIUM BUTYRICUM	2 TABLET	BID	Y-M: 20[redacted] / -112
PRANLUKAST	225 mg (milligram(s))	BID	Y-M: 20[redacted] / -112
ALFACALCIDOL	0.5 mcg (microgram(s))	QD	Y-M: 20[redacted] / -100
FAMOTIDINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -100
MESALAZINE	2000-1600 mg (milligram(s))	BID	Y-M: 20[redacted] / -100
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -99
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -85
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -69
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -55
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -36
PREDNISOLONE	3 mg (milligram(s))	QD	Y-M: 20[redacted] / -22
CARBOCISTEINE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / -6
CLARITHROMYCIN	200 mg (milligram(s))	BID	Y-M: 20[redacted] / -6
DEQUALINIUM CHLORIDE	0.25 mg (milligram(s))	PRN	Y-M: 20[redacted] / -6
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL (millilitre(s))	TID	Y-M: 20[redacted] / -2
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL (millilitre(s))	BID	Y-M: 20[redacted] / -1

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -253	ONGOING
CLOSTRIDIUM BUTYRICUM	2 TABLET	BID	Y-M: 20[redacted] / -112	ONGOING
PRANLUKAST	225 mg (milligram(s))	BID	Y-M: 20[redacted] / -112	ONGOING
MESALAZINE	2000-1600 mg (milligram(s))	BID	Y-M: 20[redacted] / -100	ONGOING
ALFACALCIDOL	0.5 mcg (microgram(s))	QD	Y-M: 20[redacted] / -100	Y-M: 20[redacted] / 71
FAMOTIDINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -100	Y-M: 20[redacted] / 71
PARACETAMOL	400 mg (milligram(s))	PRN	Y-M: 20[redacted] / 38	ONGOING
PREDNISOLONE	1 mg (milligram(s))	QD	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 71
FOSFOMYCIN CALCIUM	1000 mg (milligram(s))	TID	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 89

Event #1: Serious Adverse Event

Event Description	ENTERITIS INFECTIOUS
Preferred term	感染性腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 88): ESR1H: 24.0 [2 - 10] MM

Microbiology

[redacted]20[redacted] (RX DAY 88): Other NASAL MUCOUS MEMBRANE INFLUENZA:

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	90
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ACCIDENTAL EVENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:10:31
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男児（日本）であり，重篤な有害事象の感染性腸炎を発現した。関連する病歴は，潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎），上気道感染，慢性鼻炎及び下痢であった。

20[redacted] 年 [redacted] 月 [redacted] 日，感染性腸炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，感染性腸炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者の便の形状及び排便回数は正常であった。20[redacted] 年 [redacted] 月 [redacted] 日の朝に排便回数が増加し，便の形状は泥状となった。被験者は治験実施施設に規定外来院した。被験者によると午前中の体温は 37.6°C であったが，治験実施施設に到着時の体温は 39.0°C であった。咽頭痛，咳嗽又は鼻汁の症状はみられなかった。

発熱及び下痢の徴候及び症状が認められた。治験責任医師は，20[redacted] 年 [redacted] 月 [redacted] 日の時点で潰瘍性大腸炎の再発の可能性を否定できないと述べたが，胃腸症状の一時的な増悪は感染が原因であると判断した。外来で治療を受けながら経過観察を行うことが決定されたが，外来は休診であった。このため，20[redacted] 年 [redacted] 月 [redacted] 日に被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は解熱し，退院した。

治療薬として Fosmicin（ホスホマイシンナトリウム）が投与された。

The patient's past medications include:

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

CARBOCISTEINE for UPPER RESPIRATORYTRACT INFECTION and UPPER RESPIRATORY INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

SOLDEM 3A for PREVENTION OF DEHYDRATION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for HUMIRA (Blinded)

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1) Enteritis infectious (10058839) (Enteritis infectious (10058839)) [v.20.1] [10058839]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ENTERITIS INFECTIOUS

- Investigator: Accidental event.

- AbbVie: N/A

M11-290 試験（最終 CSR）

治験の標題： A Multicenter, Randomized, Double-Blind Study of the Human Anti-TNF Monoclonal Antibody Adalimumab in Pediatric Subjects with Moderate to Severe Ulcerative Colitis	
施設数 / 実施国名： 主試験：19 施設 / オーストリア，ベルギー，カナダ，スペイン，英国，イスラエル，ポーランド，スロバキア及び米国 日本サブ試験：5 施設 / 日本	
治験責任医師： Nicholas Croft, MD 他	
公表文献 (参考資料) ： 該当せず	
治験期間： 治験開始日（最初の被験者の初回来院日）： 主試験： 2014 年 10 月 13 日 日本サブ試験：2014 年 12 月 22 日 治験完了日（最後の被験者の最終来院日）：2020 年 2 月 7 日	開発のフェーズ： 第 III 相
治験の種類： 第 III 相，多施設共同，無作為化，二重盲検試験	
目的： 本試験の目的は，中等症から重症の小児潰瘍性大腸炎（以下「UC」）患者に対するアダリムマブの有効性及び安全性，並びにアダリムマブ皮下投与後の薬物動態について検討することである。	
被験者数 (計画時と解析時) ： 計画時 ：102 例（主試験 93 例，日本サブ試験 9 例） 組入れ時：101 例（主試験 93 例，日本サブ試験 8 例） 解析時 ：101 例（主試験 93 例，日本サブ試験 8 例）	
診断と主要な組入れ基準： 年齢が 4～17 歳の中等症から重症（副腎皮質ステロイドの経口剤若しくは免疫抑制剤又はその両方を投与しているにもかかわらず，Mayo スコア［以下「FMS」］が 6～12 ポイント，かつ内視鏡所見サブスコアが 2～3 ポイント）の小児 UC 患者で，本試験の選択基準をすべて満たし，除外基準のいずれにも抵触せず，内視鏡検査で UC の診断が確認された患者を適格とした。	

治験方法：

M11-290 試験は，副腎皮質ステロイド又は免疫抑制剤による治療が効果不十分であった中等症から重症の小児 UC 患者を対象としたアダリムマブの有効性及び安全性を評価する第 III 相多施設共同無作為化二重盲検比較試験である。本試験は，日本以外の施設で登録された被験者を対象とする主試験と，日本の施設で登録された被験者を対象とする日本サブ試験で構成される。日本サブ試験では，主試験及び日本サブ試験の結果を併合した解析と，日本の被験者のみを対象とした解析を実施した。

治験実施計画書の改訂 4 版（日本サブ試験では改訂 4.01 版；以下同様）より前に登録された被験者は，ベースライン時に 3：2 の比率でアダリムマブの導入療法期二重盲検治療群（導入療法期高用量［以下「I-HD」］又は導入療法期標準用量［以下「I-SD］）のいずれかに無作為に割り付けられた。投与 8 週時に部分的 Mayo スコア（以下「PMS」）による臨床的改善（PMS がベースラインから 2 ポイント以上かつ 30%以上減少）が認められた被験者を，2：2：1 の比率で維持療法期高用量（以下「M-HD」），維持療法期標準用量（以下「M-SD」）又は維持療法期プラセボ（以下「M-PL」）のいずれかに無作為に割り付けた。維持療法期の被験者は，投与 52 週時まで盲検下で投与を継続することとした。

治験実施計画書の改訂 4 版以降に登録された被験者には，アダリムマブ導入療法期高用量を非盲検下で投与した（導入療法期非盲検高用量［以下「I-HD-OL」］）。投与 8 週時に PMS による臨床的改善が認められた被験者を，投与 8 週時の PMS による寛解状態（PMS が 2 ポイント以下，かつ，いずれのサブスコアも 1 ポイントを超えない）を因子として層別し，1：1 の比率でアダリムマブの維持療法期治療群（M-HD 又は M-SD）のいずれかに無作為に割り付けた。維持療法期の被験者は，投与 52 週時まで盲検下で投与を継続することとした。

治験実施計画書の改訂 4 版より前は，維持療法期の対照群として内部プラセボ群を設定した。

改訂 4 版以降，規制当局との合意により，内部プラセボ群への無作為割付けを中止し，代わりに外部プラセボ群を主要有効性評価項目及び順位付き副次有効性評価項目の比較対照として用いた。

被験薬，用量，投与方法及びバッチ番号：

用量：治験実施計画書の改訂 4 版より前に I-HD 群に無作為に割り付けられた被験者には，ベースライン時及び投与 1 週時にアダリムマブ 2.4 mg/kg（最大 160 mg），投与 2 週時にアダリムマブ 1.2 mg/kg（最大 80 mg），投与 4 週時及び 6 週時にアダリムマブ 0.6 mg/kg（最大 40 mg）を投与した。I-SD 群に無作為に割り付けられた被験者には，ベースライン時にアダリムマブ 2.4 mg/kg（最大 160 mg），投与 1 週時にプラセボ，投与 2 週時にアダリムマブ 1.2 mg/kg（最大 80 mg），投与 4 週時及び 6 週時にアダリムマブ 0.6 mg/kg（最大 40 mg）を投与した。投与 8 週時に M-HD 群に無作為に割り付けられた被験者にはアダリムマブ 0.6 mg/kg（最大 40 mg）を週 1 回投与，M-SD 群に無作為に割り付けられた被験者にはアダリムマブ 0.6 mg/kg（最大 40 mg）を隔週投与した。治験実施計画書の改訂 4 版以降に登録された被験者（I-HD-OL 群）には，ベースライン時及び投与 1 週時にアダリムマブ 2.4 mg/kg（最大 160 mg），投与 2 週時にアダリムマブ 1.2 mg/kg（最大 80 mg），投与 4 週時及び 6 週時にアダリムマブ 0.6 mg/kg（最大 40 mg）を投与し，投与 8 週以降は M-HD 又は M-SD のいずれかを投与した。

投与経路：皮下投与

ロット番号：

アダリムマブ（主試験）：[redacted]

アダリムマブ（日本サブ試験）：[redacted]

プラセボ（主試験）：[redacted]

プラセボ（日本サブ試験）：[redacted]

治療期間：52 週間

対照薬，用量，投与方法及びバッチ番号：

なし

評価基準：

有効性：

主要有効性評価項目は以下のとおりであった。

- 投与 8 週時に PMS により寛解（PMS が 2 ポイント以下，かつ，いずれのサブスコアも 1 ポイントを超えない）を達成した被験者の割合
- 投与 8 週時に PMS により改善例（PMS がベースラインから 2 ポイント以上かつ 30%以上減少）となり，かつ投与 52 週時に FMS により寛解（FMS が 2 ポイント以下，かつ，いずれのサブスコアも 1 ポイントを超えない）を達成した被験者の割合

順位付き副次有効性評価項目は以下のとおりであった。

1. 投与 8 週時の PMS 改善例のうち，投与 52 週時に FMS により改善（FMS がベースラインから 3 ポイント以上かつ 30%以上減少）を達成した被験者の割合
2. 投与 8 週時の PMS 改善例のうち，投与 52 週時に Mayo 内視鏡所見サブスコアにより粘膜治癒（1 ポイント以下）が認められた被験者の割合
3. 投与 8 週時の PMS 寛解例のうち，投与 52 週時に FMS により寛解を達成した被験者の割合
4. 投与 8 週時の PMS 改善例のうち，ベースラインで副腎皮質ステロイドを投与していた被験者で，投与 52 週時以前に副腎皮質ステロイドの投与を中止し，かつ投与 52 週時に FMS により寛解を達成した被験者の割合

薬物動態：

別途報告書に記載することとした。

安全性：

治験期間中の有害事象，バイタルサインの変化，身体的所見，及び臨床検査値を評価した。

統計手法：

有効性：

投与 8 週時の有効性評価項目の解析は Intent-to-treat-E（ITT-E）集団を，投与 52 週時の有効性評価項目の解析は modified ITT-E（mITT-E）集団を対象とした。ITT-E 集団は ITT 集団のサブ集団であり，導入療法期に治験薬の投与を 1 回以上受けたすべての被験者としたが，導入療法期に非盲検下で高用量を投与された被験者は除外した。mITT-E 集団は投与 8 週時に PMS の改善が認められ，かつ投与 8 週時に無作為割付けされ，維持療法期にプラセボ以外の治験薬の投与を 1 回以上受けたすべての被験者とした。2 値変数の有効性評価項目の欠測値は，欠測値を「非反応」としてデータ補完する統計手法（以下「NRI」）を用いて補完した。導入療法期を完了しなかった被験者，又は維持療法期に救済治療を受けた被験者は，その時点以降から「無効例」として取り扱った。連続変数の有効性評価項目には，欠測値を直前の評価又は測定値でデータ補完する統計手法（以下「LOCF」）解析及び観察値（以下「OC」）解析を用いた。

主要有効性評価項目及び順位付き副次有効性評価項目のための頑健な外部プラセボを引き出すために，従来の治療が奏効しなかった中等症から重症の UC 患者を対象としたプラセボ対照臨床試験について，文献検索を実施した。複数の基準に基づき，成人を対象としたアダリムマブの試験である M06-826 試験及び M06-827 試験，並びに成人を対象とした他剤の試験である GEMINI 1 試験及び OCTAVE Sustain 試験を選択した。利用可能な場合，すべての主要有効性評価項目及び順位付け副次有効性評価項目のために，評価項目ごとに抗 TNF 製剤の投与経験の有無によるプラセボ有効率を推定するために別の評価も行った。抗 TNF 製剤の投与経験がない被験者とある被験者のプラセボ有効率の推定値を，本試験の治験実施計画書で想定した抗 TNF 製剤の投与経験がない被験者とある被験者の割合に基づいて加重平均し，統合した。より保守的にするため，加重平均値の 95%信頼区間の上限値を外部プラセボの想定として用いた。

日本サブ試験のみ

有効性の解析は，日本以外の施設で登録された被験者（主試験集団）と日本の施設で登録された被験者（日本人

集団），すなわちすべての施設で登録された被験者（統合集団），及び日本人集団を対象に実施した。

薬物動態：

別途報告書に記載することとした。

安全性：

治験薬の投与を 1 回以上受けたすべての被験者を安全性解析対象集団と定義し，安全性の解析対象とした（統合安全性解析対象集団 101 例，主試験安全性解析対象集団 93 例，日本人安全性解析対象集団 8 例）。有害事象が発現した被験者の数及び割合を，日米欧州連合（EU）医薬品ハーモナイゼーション国際会議（以下「ICH」）国際医薬品用語集（以下「MedDRA」，バージョン 22.0）の器官別大分類（以下「SOC」）及び基本語（以下「PT」）を用いて要約した。有害事象は，導入療法期中に発現したものと維持療法期中（疾患再燃が認められた場合は，再無作為化の前）に発現したものに分類した。有害事象は投与群別に記述統計量を用いて要約した。死亡に至った有害事象を含む重篤な有害事象，治験薬投与の中止に至った有害事象，及び特に注目すべき有害事象の集計表を作成した。また，有害事象の重症度別及び治験薬との因果関係別の集計表も作成した。

要約 / 結論：

有効性：

主試験

アダリムマブを高用量及び標準用量のいずれで投与した場合でも，有効性評価項目（投与 8 週時の PMS による寛解及び改善，投与 8 週時の PMS 改善例における投与 52 週時の FMS による寛解及び改善並びに粘膜治癒，投与 8 週時の PMS 寛解例における投与 52 週時の FMS による寛解など）を達成した被験者の割合は臨床的に意味のある結果と考えられた。また，小児潰瘍性大腸炎活動性指標（PUCAI）の解析結果及び医師による総合評価（PGA）を除いた FMS / PMS の解析結果からも，主要有効性評価項目及び副次有効性評価項目の結果が裏付けられた。導入療法期の主要有効性評価項目である，投与 8 週時に PMS により寛解を達成した被験者の割合は，外部プラセボよりも併合群（I-HD 群と I-SD 群），並びに I-HD 群の方が統計学的に有意に高かった。また，維持療法期の主要有効性評価項目である，投与 8 週時に PMS により改善例となり，かつ投与 52 週時に FMS により寛解を達成した被験者の割合も，外部プラセボよりも併合群（M-HD 群と M-SD 群），並びに M-HD 群の方が統計学的に有意に高かった。4 つの順位付き副次有効性評価項目（［1］投与 8 週時の PMS 改善例のうち，投与 52 週時に FMS により改善を達成した被験者の割合，［2］投与 8 週時の PMS 改善例のうち，投与 52 週時に Mayo 内視鏡所見サブスコアにより粘膜治癒が認められた被験者の割合，［3］投与 8 週時の PMS 寛解例のうち，投与 52 週時に FMS により寛解を達成した被験者の割合，並びに［4］投与 8 週時の PMS 改善例のうち，投与 52 週時以前に副腎皮質ステロイドの投与を中止し，かつ投与 52 週時に FMS により寛解を達成した被験者の割合）のうち，最初の 3 つは達成された。

アダリムマブの投与により，導入療法で PMS による改善を達成した被験者のうち，投与 52 週時以前に副腎皮質ステロイドの投与を中止し，かつ投与 52 週時に FMS により寛解を達成した被験者は約 30%であった。導入療法期及び維持療法期のいずれも，臨床反応は標準用量（I-SD 群及び M-SD 群）の投与を受けた被験者よりも，高用量（I-HD 群及び M-HD 群）の投与を受けた被験者の方が全体的に良好であった。また，有効性の結果は，抗 TNF 製剤の投与経験がある被験者よりも抗 TNF 製剤の投与経験がない被験者の方が一貫して良好であった。これらの臨床反応の改善を反映して，アダリムマブの投与を受けた被験者では，UC により入院した被験者の割合が比較的低く，結腸切除を行った被験者の割合が非常に低かった。

日本サブ試験

統合集団では，導入療法期の主要有効性評価項目である，投与 8 週時に PMS により寛解を達成した被験者の割合は，外部プラセボよりも併合群（I-HD 群と I-SD 群），並びに I-HD 群の方が統計学的に有意に高かった（統合 ITT-E 集団）。また，維持療法期の主要有効性評価項目である，投与 8 週時に PMS により改善例となり，かつ投与 52 週時に FMS により寛解を達成した被験者の割合も，外部プラセボよりも併合群（M-HD 群と M-SD 群），並びに M-HD 群の方が統計学的に有意に高かった（統合 mITT-E 集団）。日本人集団では，導入療法期の主要評価項目である投与 8 週時の主要有効性評価項目は外部プラセボよりも併合群（I-HD 群と I-SD 群），並びに I-HD 群の方が数値的に高く（日本人 ITT-E 集団），維持療法期の主要評価項目である投与 52 週時の主要有効性評価項目は外部プラセボよりも M-HD 群の方が数値的に高かった（日本人 mITT-E 集団）。

4 つの順位付き副次有効性評価項目（［1］投与 8 週時の PMS 改善例のうち，投与 52 週時に FMS により改善を達成した被験者の割合，［2］投与 8 週時の PMS 改善例のうち，投与 52 週時に Mayo 内視鏡所見サブスコアに

より粘膜治癒が認められた被験者の割合，［3］投与 8 週時の PMS 寛解例のうち，投与 52 週時に FMS により寛解を達成した被験者の割合，並びに［4］投与 8 週時の PMS 改善例のうち，投与 52 週時以前に副腎皮質ステロイドの投与を中止し，かつ投与 52 週時に FMS により寛解を達成した被験者の割合）のうち，最初の 3 つは外部プラセボよりも併合群（M-HD 群と M-SD 群），並びに M-HD 群で統計学的に有意に高かった（統合 mITT-E 集団）。

ベースライン時に副腎皮質ステロイドの投与を受け，投与 8 週時に PMS により改善例となった被験者のうち，投与 52 週時以前に副腎皮質ステロイドの投与を中止し，かつ投与 52 週時に FMS により寛解を達成した被験者の割合は，外部プラセボよりも併合群（M-HD 群と M-SD 群）（31.3%），M-HD 群（35.3%），並びに M-SD 群（26.7%）の方が数値的に高く，このうち 1 例は日本の被験者であった（M-HD 群）。また，被験者の生活の質及び介護者の仕事の生産性に意味のある改善が認められた。

統合集団では，導入療法期及び維持療法期のいずれも，臨床反応は標準用量（I-SD 群及び M-SD 群）の投与を受けた被験者よりも，高用量（I-HD 群及び M-HD 群）の投与を受けた被験者の方が全体的に良好であった。また，有効性の結果は，抗 TNF 製剤の投与経験がある被験者よりも抗 TNF 製剤の投与経験がない被験者の方が一貫して良好であった。これらの臨床反応の改善を反映して，いずれのアダリムマブ投与群でも，治験期間中に UC により入院した被験者の割合は比較的低かった（20%未満）。統合集団のうち，日本以外の被験者 2 例が治験期間中に結腸切除を行った。日本人集団では，導入療法期中及び維持療法期中にそれぞれ 1 例が UC により入院した。日本人 ITT-E 集団及び日本人 mITT-E 集団の有効性の結果は，統合 ITT-E 集団及び統合 mITT-E 集団の結果とそれぞれ一致していた。

安全性：

主試験

疾患再燃後のアダリムマブによる救済治療を含め，アダリムマブの投与を受けた主試験安全性解析対象集団の被験者 93 例中 73 例（78.5%）に 1 件以上の有害事象が発現した。死亡又は悪性腫瘍は認められなかった。重篤な有害事象及び治験薬投与の中止に至った有害事象の発現割合は低く，認められた事象は基礎疾患から予想されるものであった。

導入療法期中の有害事象の発現割合は，I-SD 群と I-HD 群で同程度であった。重篤な有害事象，高度の有害事象，治験薬投与の中止に至った有害事象の発現割合は，I-SD 群の方が I-HD 群よりも若干高かった。ただし，被験者数が少ないため，解釈には注意が必要である。維持療法期中（最初の疾患再燃前）の有害事象の発現割合は，M-SD 群と M-HD 群で同程度であった。高度の有害事象及び治験薬投与の中止に至った有害事象の発現割合は，M-SD 群の方が M-HD 群よりも高かった。ただし，被験者数が少ないため，治験薬投与の中止に至った有害事象の解釈には注意が必要である。また，重篤な有害事象の 100 人年当たりの発現率は，アダリムマブの投与を標準用量で受けた被験者の方が高用量で受けた被験者よりも高く，発現した重篤な有害事象の約半数は UC に関連する事象であった。

導入療法期及び維持療法期のいずれも，治験責任医師により治験薬と関連ありと判断された有害事象の発現割合は低く，I-SD 群と I-HD 群，M-SD 群と M-HD 群でそれぞれ同程度であった。治験期間中に認められた有害事象の大部分は重症度が軽度又は中等度であった。

特に注目すべき有害事象の発現割合は，感染症を除き全体的に低かった。感染症の大部分は重症度が軽度かつ非重篤で，容易に管理可能であった。特に注目すべき有害事象の発現割合は投与群間でおおむね同程度であった。ただし，血液障害及び注射部位反応の発現割合は M-SD 群の方が M-HD 群よりも高かった。

治験期間中の血液学的検査，血液生化学検査及び尿検査の平均値の変化は臨床的に重要ではないと判断された。また，導入療法期及び維持療法期のいずれも，血液学的検査値，血液生化学検査値及び尿検査値に関して，ベースラインが正常値若しくは異常高値であった検査値が最終測定時に異常低値に変動した被験者，ベースラインが異常低値若しくは正常値であった検査値が最終測定時に異常高値に変動した被験者，又は共通毒性基準（以下「CTC」）グレードがベースラインから悪化した被験者は全般的に少数であり，臨床的に重要ではないと判断された。治験期間中，臨床的に意味のある（CTC グレード 3 以上）血液学的検査値が認められた被験者は少数であり，臨床的に重要ではないと判断された。臨床的に意味のある（CTC グレード 3 以上）血液生化学検査値は認められなかった。臨床的に意味のある肝機能検査値が認められた被験者は少数であり，臨床的に重要ではないと判断された。Hy's law の基準に該当した被験者は認められなかった。

バイタルサインの平均値のベースラインからの変化は臨床的に重要ではないと判断された。

治験期間中，妊娠は報告されなかった。すべての治験薬に係る苦情を評価した結果，治験期間中に安全性に関する新たなリスクは特定されなかった。

治験期間全体で，中等症から重症の小児 UC 患者に対するアダリムマブ投与の安全性及び忍容性は良好であった。本試験で認められたアダリムマブの安全性プロファイルは，様々な適応症で確立されているアダリムマブの安全性プロファイルと一致しており，基礎疾患から予想されるものであった。

日本サブ試験

疾患再燃後のアダリムマブによる救済治療を含め，アダリムマブの投与を受けた統合安全性解析対象集団の被験者 101 例中 81 例（80.2%）に 1 件以上の有害事象が発現した。死亡，悪性腫瘍，活動性結核又は脱髄疾患は認められなかった。重篤な有害事象及び治験薬投与の中止に至った有害事象の発現割合は低く，認められた事象は基礎疾患から予想されるものであった。

導入療法期中の有害事象の発現割合は，I-SD 群と I-HD 群で同程度であった（統合安全性解析対象集団）。重篤な有害事象，高度の有害事象，治験薬投与の中止に至った有害事象の発現割合は，I-SD 群の方が I-HD 群よりも若干高かった。ただし，被験者数が少ないため，解釈には注意が必要である。維持療法期中（最初の疾患再燃前）の有害事象の発現割合は，M-SD 群と M-HD 群で同程度であった。高度の有害事象及び治験薬投与の中止に至った有害事象の発現割合は，M-SD 群の方が M-HD 群よりも高かった。ただし，被験者数が少ないため，治験薬投与の中止に至った有害事象の解釈には注意が必要である。また，重篤な有害事象の 100 人年当たりの発現率は，アダリムマブの投与を標準用量で受けた被験者の方が高用量で受けた被験者よりも高く，導入療法期と維持療法期で最も多く発現した重篤な有害事象は UC に関連する事象であった。日本人安全性解析対象集団では，導入療法期中に重篤な有害事象は発現せず，治験薬投与の中止に至った有害事象が I-SD 群の 1 例に発現した。また，維持療法期中に重篤な有害事象が M-SD 群の 1 例に発現した。

導入療法期及び維持療法期のいずれも，治験責任医師により治験薬と関連ありと判断された有害事象の発現割合は低く，I-SD 群と I-HD 群，M-SD 群と M-HD 群でそれぞれ同程度であった（統合安全性解析対象集団）。導入療法期及び維持療法期のいずれも，感染症を除く有害事象の重症度は大部分が軽度又は中等度であった（統合安全性解析対象集団）。

感染症の大部分は重症度が軽度かつ非重篤で，自然治癒性又は容易に管理可能であった。他の特に注目すべき有害事象の発現割合は投与群間でおおむね同程度であった。維持療法期中（最初の疾患再燃前），M-HD 群の 1 例で潜在性結核が認められた。日本人安全性解析対象集団で認められた特に注目すべき有害事象は，感染症及び注射部位反応のみであった。

治験期間中の血液学的検査，血液生化学検査及び尿検査の平均値の変化は臨床的に重要ではないと判断された。また，導入療法期及び維持療法期のいずれも，血液学的検査値及び血液生化学検査値に関して，ベースラインが正常値若しくは異常高値であった検査値が最終測定時に異常低値に変動した被験者，及びベースラインが異常低値若しくは正常値であった検査値が最終測定時に異常高値に変動した被験者は全般的に少数であり，臨床的に重要ではないと判断された。Hy's law の基準に該当した被験者は認められなかった。

治験期間中，妊娠は報告されなかった。すべての治験薬に係る苦情を評価した結果，治験期間中に安全性に関する新たなリスクは特定されなかった。

中等症から重症の小児 UC 患者にアダリムマブを 52 週間投与した結果，安全性及び忍容性は良好であった。日本人集団の安全性の結果は，統合集団の結果と一致していた。本試験で認められたアダリムマブの安全性プロファイルは，様々な適応症で確立されているアダリムマブの安全性プロファイルと一致しており，基礎疾患から予想されるものであった。

結論：

主要有効性評価項目，及び 4 つの順位付き副次有効性評価項目のうち最初の 3 つの結果に基づき，中等症から重症の小児 UC 患者における，アダリムマブの標準用量及び高用量の導入療法期での臨床的有効性，並びに維持療法期での改善及び寛解の維持効果が裏付けられた。全体的にアダリムマブの安全性及び忍容性は良好で，安全性プロファイルは過去のアダリムマブの臨床試験で確立されているものと一致しており，新たな安全性シグナルは認められなかった。日本人集団における有効性及び安全性の結果は，統合集団（日本以外の施設で登録された被験者と日本の施設で登録された被験者を統合）の結果と一致していた。

表 1. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
Any adverse event	17 (56.7)	23 (48.9)	12 (75.0)	52 (55.9)
血液およびリンパ系障害	3 (10.0)	3 (6.4)	1 (6.3)	7 (7.5)
貧血	3 (10.0)	3 (6.4)	1 (6.3)	7 (7.5)
血小板増加症	0	0	1 (6.3)	1 (1.1)
心臓障害	1 (3.3)	0	0	1 (1.1)
心膜炎	1 (3.3)	0	0	1 (1.1)
内分泌障害	1 (3.3)	0	0	1 (1.1)
甲状腺腫	1 (3.3)	0	0	1 (1.1)
眼障害	1 (3.3)	0	0	1 (1.1)
角膜炎	1 (3.3)	0	0	1 (1.1)
胃腸障害	6 (20.0)	9 (19.1)	5 (31.3)	20 (21.5)
腹痛	0	2 (4.3)	2 (12.5)	4 (4.3)
上腹部痛	1 (3.3)	2 (4.3)	0	3 (3.2)
潰瘍性大腸炎	4 (13.3)	2 (4.3)	1 (6.3)	7 (7.5)
便秘	0	0	1 (6.3)	1 (1.1)
下痢	0	0	1 (6.3)	1 (1.1)
血性下痢	1 (3.3)	0	0	1 (1.1)
小腸炎	1 (3.3)	0	0	1 (1.1)
鼓腸	1 (3.3)	0	0	1 (1.1)
排便回数増加	0	1 (2.1)	0	1 (1.1)
胃食道逆流性疾患	0	1 (2.1)	1 (6.3)	2 (2.2)

表 1. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
胃腸障害 (Cont.)				
血便排泄	0	2 (4.3)	0	2 (2.2)
悪心	0	3 (6.4)	1 (6.3)	4 (4.3)
膵炎	0	1 (2.1)	0	1 (1.1)
嘔吐	0	1 (2.1)	1 (6.3)	2 (2.2)
一般・全身障害および投与部位の状態	3 (10.0)	6 (12.8)	0	9 (9.7)
腋窩痛	0	1 (2.1)	0	1 (1.1)
胸痛	0	1 (2.1)	0	1 (1.1)
疲労	0	1 (2.1)	0	1 (1.1)
注射部位疼痛	0	1 (2.1)	0	1 (1.1)
注射部位蕁麻疹	0	1 (2.1)	0	1 (1.1)
末梢腫脹	1 (3.3)	0	0	1 (1.1)
発熱	2 (6.7)	1 (2.1)	0	3 (3.2)
肝胆道系障害	1 (3.3)	0	0	1 (1.1)
高ビリルビン血症	1 (3.3)	0	0	1 (1.1)
感染症および寄生虫症	6 (20.0)	8 (17.0)	6 (37.5)	20 (21.5)
気管支炎	0	0	1 (6.3)	1 (1.1)
せつ	0	1 (2.1)	0	1 (1.1)
サルモネラ菌性胃腸炎	1 (3.3)	0	0	1 (1.1)
上咽頭炎	2 (6.7)	2 (4.3)	1 (6.3)	5 (5.4)
口腔ヘルペス	1 (3.3)	2 (4.3)	0	3 (3.2)
咽頭炎	2 (6.7)	1 (2.1)	1 (6.3)	4 (4.3)

表 1. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
感染症および寄生虫症 (Cont.)				
レンサ球菌感染	0	0	1 (6.3)	1 (1.1)
上気道感染	0	1 (2.1)	0	1 (1.1)
尿路感染	1 (3.3)	0	0	1 (1.1)
水痘	0	1 (2.1)	0	1 (1.1)
ウイルス感染	0	0	1 (6.3)	1 (1.1)
ウイルス性上気道感染	0	1 (2.1)	0	1 (1.1)
外陰腟真菌感染	0	0	1 (6.3)	1 (1.1)
傷害、中毒および処置合併症	4 (13.3)	2 (4.3)	0	6 (6.5)
節足動物咬傷	1 (3.3)	0	0	1 (1.1)
転倒	1 (3.3)	0	0	1 (1.1)
注入に伴う反応	1 (3.3)	0	0	1 (1.1)
靭帯捻挫	1 (3.3)	0	0	1 (1.1)
処置による疼痛	0	1 (2.1)	0	1 (1.1)
手首関節骨折	0	1 (2.1)	0	1 (1.1)
臨床検査	2 (6.7)	2 (4.3)	1 (6.3)	5 (5.4)
血圧上昇	0	1 (2.1)	0	1 (1.1)
C－反応性蛋白増加	0	1 (2.1)	0	1 (1.1)
ヘモグロビン減少	1 (3.3)	0	0	1 (1.1)
肝酵素上昇	0	0	1 (6.3)	1 (1.1)
体重減少	1 (3.3)	1 (2.1)	0	2 (2.2)

表 1. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
筋骨格系および結合組織障害	2 (6.7)	2 (4.3)	1 (6.3)	5 (5.4)
関節痛	1 (3.3)	0	1 (6.3)	2 (2.2)
背部痛	0	1 (2.1)	0	1 (1.1)
靭帯障害	0	1 (2.1)	0	1 (1.1)
四肢痛	1 (3.3)	0	0	1 (1.1)
神経系障害	5 (16.7)	5 (10.6)	4 (25.0)	14 (15.1)
頭痛	4 (13.3)	5 (10.6)	4 (25.0)	13 (14.0)
意識消失	1 (3.3)	0	0	1 (1.1)
片頭痛	1 (3.3)	0	0	1 (1.1)
錯感覚	1 (3.3)	0	0	1 (1.1)
振戦	0	1 (2.1)	1 (6.3)	2 (2.2)
腎および尿路障害	0	0	1 (6.3)	1 (1.1)
糖尿	0	0	1 (6.3)	1 (1.1)
生殖系および乳房障害	0	1 (2.1)	0	1 (1.1)
乳房痛	0	1 (2.1)	0	1 (1.1)
呼吸器、胸郭および縦隔障害	1 (3.3)	3 (6.4)	3 (18.8)	7 (7.5)
咳嗽	0	1 (2.1)	0	1 (1.1)
鼻閉	0	1 (2.1)	0	1 (1.1)
口腔咽頭痛	1 (3.3)	1 (2.1)	2 (12.5)	4 (4.3)
鼻漏	0	1 (2.1)	1 (6.3)	2 (2.2)

表 1. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
皮膚および皮下組織障害	1 (3.3)	0	1 (6.3)	2 (2.2)
結節性紅斑	1 (3.3)	0	0	1 (1.1)
発疹	0	0	1 (6.3)	1 (1.1)

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.1.1.1

表 2. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	19 (59.4)	27 (52.9)	14 (77.8)	60 (59.4)
血液およびリンパ系障害	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
貧血	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
血小板増加症	0	0	1 (5.6)	1 (1.0)
心臓障害	1 (3.1)	0	0	1 (1.0)
心膜炎	1 (3.1)	0	0	1 (1.0)
内分泌障害	1 (3.1)	0	0	1 (1.0)
甲状腺腫	1 (3.1)	0	0	1 (1.0)
眼障害	1 (3.1)	1 (2.0)	0	2 (2.0)
眼瞼炎	0	1 (2.0)	0	1 (1.0)
角膜炎	1 (3.1)	0	0	1 (1.0)
胃腸障害	6 (18.8)	9 (17.6)	5 (27.8)	20 (19.8)
腹痛	0	2 (3.9)	2 (11.1)	4 (4.0)
上腹部痛	1 (3.1)	2 (3.9)	0	3 (3.0)
潰瘍性大腸炎	4 (12.5)	2 (3.9)	1 (5.6)	7 (6.9)
便秘	0	0	1 (5.6)	1 (1.0)
下痢	0	0	1 (5.6)	1 (1.0)
血性下痢	1 (3.1)	0	0	1 (1.0)
小腸炎	1 (3.1)	0	0	1 (1.0)
鼓腸	1 (3.1)	0	0	1 (1.0)

表 2. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
胃腸障害 (Cont.)				
排便回数増加	0	1 (2.0)	0	1 (1.0)
胃食道逆流性疾患	0	1 (2.0)	1 (5.6)	2 (2.0)
血便排泄	0	2 (3.9)	0	2 (2.0)
悪心	0	3 (5.9)	1 (5.6)	4 (4.0)
膵炎	0	1 (2.0)	0	1 (1.0)
嘔吐	0	1 (2.0)	1 (5.6)	2 (2.0)
一般・全身障害および投与部位の状態	5 (15.6)	7 (13.7)	1 (5.6)	13 (12.9)
腋窩痛	0	1 (2.0)	0	1 (1.0)
胸痛	0	1 (2.0)	0	1 (1.0)
疲労	0	1 (2.0)	0	1 (1.0)
異常感	1 (3.1)	0	0	1 (1.0)
注射部位紅斑	0	1 (2.0)	0	1 (1.0)
注射部位疼痛	1 (3.1)	1 (2.0)	0	2 (2.0)
注射部位蕁麻疹	0	1 (2.0)	0	1 (1.0)
末梢腫脹	1 (3.1)	0	1 (5.6)	2 (2.0)
発熱	2 (6.3)	1 (2.0)	0	3 (3.0)
肝胆道系障害	1 (3.1)	0	0	1 (1.0)
高ビリルビン血症	1 (3.1)	0	0	1 (1.0)
感染症および寄生虫症	6 (18.8)	11 (21.6)	6 (33.3)	23 (22.8)
気管支炎	0	0	1 (5.6)	1 (1.0)

表 2. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
感染症および寄生虫症 (Cont.)				
せつ	0	1 (2.0)	0	1 (1.0)
サルモネラ菌性胃腸炎	1 (3.1)	0	0	1 (1.0)
上咽頭炎	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
口腔ヘルペス	1 (3.1)	2 (3.9)	0	3 (3.0)
外耳炎	0	1 (2.0)	0	1 (1.0)
咽頭炎	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
レンサ球菌感染	0	0	1 (5.6)	1 (1.0)
上気道感染	0	3 (5.9)	0	3 (3.0)
尿路感染	1 (3.1)	0	0	1 (1.0)
水痘	0	1 (2.0)	0	1 (1.0)
ウイルス感染	0	0	1 (5.6)	1 (1.0)
ウイルス性上気道感染	0	1 (2.0)	0	1 (1.0)
外陰腟真菌感染	0	0	1 (5.6)	1 (1.0)
傷害、中毒および処置合併症	4 (12.5)	2 (3.9)	0	6 (5.9)
節足動物咬傷	1 (3.1)	0	0	1 (1.0)
転倒	1 (3.1)	0	0	1 (1.0)
注入に伴う反応	1 (3.1)	0	0	1 (1.0)
靱帯捻挫	1 (3.1)	0	0	1 (1.0)
処置による疼痛	0	1 (2.0)	0	1 (1.0)
手首関節骨折	0	1 (2.0)	0	1 (1.0)

表 2. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
臨床検査	2 (6.3)	2 (3.9)	2 (11.1)	6 (5.9)
血圧上昇	0	1 (2.0)	0	1 (1.0)
C－反応性蛋白増加	0	1 (2.0)	0	1 (1.0)
ヘモグロビン減少	1 (3.1)	0	0	1 (1.0)
肝酵素上昇	0	0	1 (5.6)	1 (1.0)
単球数減少	0	0	1 (5.6)	1 (1.0)
好中球数減少	0	0	1 (5.6)	1 (1.0)
体重減少	1 (3.1)	1 (2.0)	0	2 (2.0)
白血球数減少	0	0	1 (5.6)	1 (1.0)
筋骨格系および結合組織障害	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
関節痛	1 (3.1)	0	1 (5.6)	2 (2.0)
背部痛	0	1 (2.0)	0	1 (1.0)
靱帯障害	0	1 (2.0)	0	1 (1.0)
四肢痛	1 (3.1)	0	0	1 (1.0)
神経系障害	6 (18.8)	5 (9.8)	4 (22.2)	15 (14.9)
頭痛	5 (15.6)	5 (9.8)	4 (22.2)	14 (13.9)
意識消失	1 (3.1)	0	0	1 (1.0)
片頭痛	1 (3.1)	0	0	1 (1.0)
錯感覚	1 (3.1)	0	0	1 (1.0)
振戦	0	1 (2.0)	1 (5.6)	2 (2.0)

表 2. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
腎および尿路障害	0	0	1 (5.6)	1 (1.0)
糖尿	0	0	1 (5.6)	1 (1.0)
生殖系および乳房障害	0	1 (2.0)	0	1 (1.0)
乳房痛	0	1 (2.0)	0	1 (1.0)
呼吸器、胸郭および縦隔障害	1 (3.1)	3 (5.9)	3 (16.7)	7 (6.9)
咳嗽	0	1 (2.0)	0	1 (1.0)
鼻閉	0	1 (2.0)	0	1 (1.0)
口腔咽頭痛	1 (3.1)	1 (2.0)	2 (11.1)	4 (4.0)
鼻漏	0	1 (2.0)	1 (5.6)	2 (2.0)
皮膚および皮下組織障害	1 (3.1)	0	1 (5.6)	2 (2.0)
結節性紅斑	1 (3.1)	0	0	1 (1.0)
発疹	0	0	1 (5.6)	1 (1.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.1.1.1_A

表 3. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
Any adverse event	2 (100)	4 (100)	2 (100)	8 (100)
眼障害	0	1 (25.0)	0	1 (12.5)
眼瞼炎	0	1 (25.0)	0	1 (12.5)
一般・全身障害および投与部位の状態	2 (100)	1 (25.0)	1 (50.0)	4 (50.0)
異常感	1 (50.0)	0	0	1 (12.5)
注射部位紅斑	0	1 (25.0)	0	1 (12.5)
注射部位疼痛	1 (50.0)	0	0	1 (12.5)
末梢腫脹	0	0	1 (50.0)	1 (12.5)
感染症および寄生虫症	0	3 (75.0)	0	3 (37.5)
外耳炎	0	1 (25.0)	0	1 (12.5)
上気道感染	0	2 (50.0)	0	2 (25.0)
臨床検査	0	0	1 (50.0)	1 (12.5)
単球数減少	0	0	1 (50.0)	1 (12.5)
好中球数減少	0	0	1 (50.0)	1 (12.5)
白血球数減少	0	0	1 (50.0)	1 (12.5)
神経系障害	1 (50.0)	0	0	1 (12.5)
頭痛	1 (50.0)	0	0	1 (12.5)

表 3. 導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（日本人安全性解析対象集団，M11-290 試験）（続き）

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.1.1.1_J

表 4. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
Any adverse event	20 (64.5)	22 (68.8)	42 (66.7)	10 (83.3)	52 (69.3)
血液およびリンパ系障害	4 (12.9)	1 (3.1)	5 (7.9)	2 (16.7)	7 (9.3)
貧血	3 (9.7)	1 (3.1)	4 (6.3)	1 (8.3)	5 (6.7)
リンパ節症	1 (3.2)	0	1 (1.6)	0	1 (1.3)
好中球減少症	0	0	0	1 (8.3)	1 (1.3)
耳および迷路障害	0	1 (3.1)	1 (1.6)	0	1 (1.3)
耳痛	0	1 (3.1)	1 (1.6)	0	1 (1.3)
眼障害	0	0	0	1 (8.3)	1 (1.3)
非感染性結膜炎	0	0	0	1 (8.3)	1 (1.3)
胃腸障害	9 (29.0)	10 (31.3)	19 (30.2)	3 (25.0)	22 (29.3)
腹痛	1 (3.2)	1 (3.1)	2 (3.2)	1 (8.3)	3 (4.0)
上腹部痛	0	2 (6.3)	2 (3.2)	0	2 (2.7)
アフタ性潰瘍	1 (3.2)	0	1 (1.6)	0	1 (1.3)
潰瘍性大腸炎	6 (19.4)	4 (12.5)	10 (15.9)	2 (16.7)	12 (16.0)
便秘	1 (3.2)	0	1 (1.6)	0	1 (1.3)
下痢	0	1 (3.1)	1 (1.6)	0	1 (1.3)
消化不良	0	1 (3.1)	1 (1.6)	0	1 (1.3)
小腸炎	2 (6.5)	1 (3.1)	3 (4.8)	0	3 (4.0)
胃食道逆流性疾患	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 4. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
一般・全身障害および投与部位の状態	5 (16.1)	3 (9.4)	8 (12.7)	1 (8.3)	9 (12.0)
胸痛	0	1 (3.1)	1 (1.6)	0	1 (1.3)
疲労	2 (6.5)	0	2 (3.2)	0	2 (2.7)
炎症	0	0	0	1 (8.3)	1 (1.3)
注射部位紅斑	0	1 (3.1)	1 (1.6)	0	1 (1.3)
注射部位炎症	1 (3.2)	0	1 (1.6)	0	1 (1.3)
注射部位浮腫	1 (3.2)	0	1 (1.6)	0	1 (1.3)
注射部位疼痛	1 (3.2)	0	1 (1.6)	0	1 (1.3)
注射部位そう痒感	0	1 (3.1)	1 (1.6)	0	1 (1.3)
注射部位腫脹	1 (3.2)	0	1 (1.6)	0	1 (1.3)
注射部位蕁麻疹	0	1 (3.1)	1 (1.6)	0	1 (1.3)
倦怠感	0	1 (3.1)	1 (1.6)	0	1 (1.3)
発熱	1 (3.2)	0	1 (1.6)	0	1 (1.3)
免疫系障害	0	1 (3.1)	1 (1.6)	0	1 (1.3)
薬物過敏症	0	1 (3.1)	1 (1.6)	0	1 (1.3)
感染症および寄生虫症	10 (32.3)	13 (40.6)	23 (36.5)	5 (41.7)	28 (37.3)
気管支炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
胃腸炎	2 (6.5)	0	2 (3.2)	1 (8.3)	3 (4.0)
感染性嚢腫	0	1 (3.1)	1 (1.6)	0	1 (1.3)
インフルエンザ	0	1 (3.1)	1 (1.6)	0	1 (1.3)
喉頭炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 4. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
感染症および寄生虫症 (Cont.)					
無菌性髄膜炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
上咽頭炎	3 (9.7)	4 (12.5)	7 (11.1)	1 (8.3)	8 (10.7)
口腔ヘルペス	0	1 (3.1)	1 (1.6)	0	1 (1.3)
中耳炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
咽頭炎	2 (6.5)	2 (6.3)	4 (6.3)	1 (8.3)	5 (6.7)
気道感染	1 (3.2)	0	1 (1.6)	0	1 (1.3)
ウイルス性気道感染	0	0	0	1 (8.3)	1 (1.3)
鼻炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
癜風	1 (3.2)	0	1 (1.6)	0	1 (1.3)
歯膿瘍	0	0	0	1 (8.3)	1 (1.3)
気管炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
上気道感染	2 (6.5)	3 (9.4)	5 (7.9)	2 (16.7)	7 (9.3)
尿路感染	1 (3.2)	2 (6.3)	3 (4.8)	0	3 (4.0)
水痘	0	1 (3.1)	1 (1.6)	0	1 (1.3)
傷害、中毒および処置合併症	0	1 (3.1)	1 (1.6)	1 (8.3)	2 (2.7)
手骨折	0	1 (3.1)	1 (1.6)	0	1 (1.3)
関節損傷	0	0	0	1 (8.3)	1 (1.3)
臨床検査	5 (16.1)	3 (9.4)	8 (12.7)	0	8 (10.7)
血中ビリルビン増加	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
血中カルシウム減少	1 (3.2)	0	1 (1.6)	0	1 (1.3)
血中ナトリウム減少	0	1 (3.1)	1 (1.6)	0	1 (1.3)
骨密度減少	1 (3.2)	0	1 (1.6)	0	1 (1.3)

表 4. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
C－反応性蛋白増加	3 (9.7)	0	3 (4.8)	0	3 (4.0)
好酸球数増加	0	1 (3.1)	1 (1.6)	0	1 (1.3)
リンパ節触知	1 (3.2)	0	1 (1.6)	0	1 (1.3)
結核菌群検査陽性	0	1 (3.1)	1 (1.6)	0	1 (1.3)
好中球数減少	1 (3.2)	0	1 (1.6)	0	1 (1.3)
白血球数減少	1 (3.2)	0	1 (1.6)	0	1 (1.3)
筋骨格系および結合組織障害	1 (3.2)	2 (6.3)	3 (4.8)	1 (8.3)	4 (5.3)
関節痛	0	1 (3.1)	1 (1.6)	0	1 (1.3)
背部痛	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
筋骨格痛	0	0	0	1 (8.3)	1 (1.3)
神経系障害	6 (19.4)	3 (9.4)	9 (14.3)	2 (16.7)	11 (14.7)
頭痛	6 (19.4)	2 (6.3)	8 (12.7)	2 (16.7)	10 (13.3)
感覚鈍麻	0	1 (3.1)	1 (1.6)	0	1 (1.3)
錯感覚	0	1 (3.1)	1 (1.6)	0	1 (1.3)
精神障害	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
うつ病	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
生殖系および乳房障害	0	1 (3.1)	1 (1.6)	0	1 (1.3)
月経困難症	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 4. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
呼吸器、胸郭および縦隔障害	4 (12.9)	5 (15.6)	9 (14.3)	3 (25.0)	12 (16.0)
喘息	1 (3.2)	0	1 (1.6)	0	1 (1.3)
咳嗽	0	2 (6.3)	2 (3.2)	0	2 (2.7)
鼻出血	0	0	0	2 (16.7)	2 (2.7)
鼻浮腫	1 (3.2)	0	1 (1.6)	0	1 (1.3)
口腔咽頭痛	2 (6.5)	1 (3.1)	3 (4.8)	0	3 (4.0)
アレルギー性鼻炎	0	2 (6.3)	2 (3.2)	0	2 (2.7)
鼻漏	1 (3.2)	0	1 (1.6)	0	1 (1.3)
喘鳴	0	0	0	1 (8.3)	1 (1.3)
皮膚および皮下組織障害	1 (3.2)	6 (18.8)	7 (11.1)	3 (25.0)	10 (13.3)
脱毛症	0	1 (3.1)	1 (1.6)	0	1 (1.3)
皮膚炎	0	1 (3.1)	1 (1.6)	1 (8.3)	2 (2.7)
紅斑	0	1 (3.1)	1 (1.6)	0	1 (1.3)
結節性紅斑	0	1 (3.1)	1 (1.6)	0	1 (1.3)
逆むけ	0	0	0	1 (8.3)	1 (1.3)
乾癬	0	0	0	1 (8.3)	1 (1.3)
発疹	1 (3.2)	2 (6.3)	3 (4.8)	0	3 (4.0)
痂皮	0	1 (3.1)	1 (1.6)	0	1 (1.3)
脂漏	1 (3.2)	0	1 (1.6)	0	1 (1.3)
皮膚病変	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 4.　　維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.1.1.2

表 5. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	21 (63.6)	26 (72.2)	47 (68.1)	10 (83.3)	57 (70.4)
血液およびリンパ系障害	4 (12.1)	1 (2.8)	5 (7.2)	2 (16.7)	7 (8.6)
貧血	3 (9.1)	1 (2.8)	4 (5.8)	1 (8.3)	5 (6.2)
リンパ節症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
好中球減少症	0	0	0	1 (8.3)	1 (1.2)
耳および迷路障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
耳痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
眼障害	0	0	0	1 (8.3)	1 (1.2)
非感染性結膜炎	0	0	0	1 (8.3)	1 (1.2)
胃腸障害	9 (27.3)	10 (27.8)	19 (27.5)	3 (25.0)	22 (27.2)
腹痛	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
上腹部痛	0	2 (5.6)	2 (2.9)	0	2 (2.5)
アフタ性潰瘍	1 (3.0)	0	1 (1.4)	0	1 (1.2)
潰瘍性大腸炎	6 (18.2)	4 (11.1)	10 (14.5)	2 (16.7)	12 (14.8)
便秘	1 (3.0)	0	1 (1.4)	0	1 (1.2)
下痢	0	1 (2.8)	1 (1.4)	0	1 (1.2)
消化不良	0	1 (2.8)	1 (1.4)	0	1 (1.2)
小腸炎	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
胃食道逆流性疾患	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 5. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
一般・全身障害および投与部位の状態	5 (15.2)	3 (8.3)	8 (11.6)	1 (8.3)	9 (11.1)
胸痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
疲労	2 (6.1)	0	2 (2.9)	0	2 (2.5)
炎症	0	0	0	1 (8.3)	1 (1.2)
注射部位紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位炎症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位疼痛	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位そう痒感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位腫脹	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位蕁麻疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)
倦怠感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発熱	1 (3.0)	0	1 (1.4)	0	1 (1.2)
免疫系障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
薬物過敏症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染症および寄生虫症	11 (33.3)	17 (47.2)	28 (40.6)	5 (41.7)	33 (40.7)
気管支炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
結膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染性腸炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
胃腸炎	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
膿痂疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 5. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
感染性嚢腫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
インフルエンザ	0	2 (5.6)	2 (2.9)	0	2 (2.5)
喉頭炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
無菌性髄膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
上咽頭炎	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)	8 (9.9)
口腔ヘルペス	0	1 (2.8)	1 (1.4)	0	1 (1.2)
中耳炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
咽頭炎	2 (6.1)	2 (5.6)	4 (5.8)	1 (8.3)	5 (6.2)
気道感染	1 (3.0)	0	1 (1.4)	0	1 (1.2)
ウイルス性気道感染	0	0	0	1 (8.3)	1 (1.2)
鼻炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
癜風	1 (3.0)	0	1 (1.4)	0	1 (1.2)
歯膿瘍	0	0	0	1 (8.3)	1 (1.2)
気管炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
上気道感染	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)	8 (9.9)
尿路感染	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
水痘	0	1 (2.8)	1 (1.4)	0	1 (1.2)
傷害、中毒および処置合併症	0	3 (8.3)	3 (4.3)	1 (8.3)	4 (4.9)
眼瞼挫傷	0	1 (2.8)	1 (1.4)	0	1 (1.2)
手骨折	0	2 (5.6)	2 (2.9)	0	2 (2.5)

表 5. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
傷害、中毒および処置合併症 (Cont.)					
関節損傷	0	0	0	1 (8.3)	1 (1.2)
靭帯捻挫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
臨床検査	5 (15.2)	3 (8.3)	8 (11.6)	0	8 (9.9)
血中ビリルビン増加	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
血中カルシウム減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
血中ナトリウム減少	0	1 (2.8)	1 (1.4)	0	1 (1.2)
骨密度減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
C一反応性蛋白増加	3 (9.1)	0	3 (4.3)	0	3 (3.7)
好酸球数増加	0	1 (2.8)	1 (1.4)	0	1 (1.2)
リンパ節触知	1 (3.0)	0	1 (1.4)	0	1 (1.2)
結核菌群検査陽性	0	1 (2.8)	1 (1.4)	0	1 (1.2)
好中球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
白血球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
筋骨格系および結合組織障害	1 (3.0)	2 (5.6)	3 (4.3)	1 (8.3)	4 (4.9)
関節痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
背部痛	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
筋骨格痛	0	0	0	1 (8.3)	1 (1.2)
神経系障害	6 (18.2)	3 (8.3)	9 (13.0)	2 (16.7)	11 (13.6)
頭痛	6 (18.2)	2 (5.6)	8 (11.6)	2 (16.7)	10 (12.3)
感覚鈍麻	0	1 (2.8)	1 (1.4)	0	1 (1.2)
錯感覚	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 5. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
精神障害	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
うつ病	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
生殖系および乳房障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
月経困難症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
呼吸器、胸郭および縦隔障害	4 (12.1)	5 (13.9)	9 (13.0)	3 (25.0)	12 (14.8)
喘息	1 (3.0)	0	1 (1.4)	0	1 (1.2)
咳嗽	0	2 (5.6)	2 (2.9)	0	2 (2.5)
鼻出血	0	0	0	2 (16.7)	2 (2.5)
鼻浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
口腔咽頭痛	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
アレルギー性鼻炎	0	2 (5.6)	2 (2.9)	0	2 (2.5)
鼻漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
喘鳴	0	0	0	1 (8.3)	1 (1.2)
皮膚および皮下組織障害	1 (3.0)	7 (19.4)	8 (11.6)	3 (25.0)	11 (13.6)
脱毛症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
皮膚炎	0	1 (2.8)	1 (1.4)	1 (8.3)	2 (2.5)
紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
結節性紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
逆むけ	0	0	0	1 (8.3)	1 (1.2)

表 5. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
皮膚および皮下組織障害 (Cont.)					
乾癬	0	0	0	1 (8.3)	1 (1.2)
紫斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発疹	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
痂皮	0	1 (2.8)	1 (1.4)	0	1 (1.2)
脂漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
皮膚病変	0	1 (2.8)	1 (1.4)	0	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.1.1.2_A

表 6. 維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total-ADA (N=6) n (%)	M-PL (N=0) n (%)	Total (N=6) n (%)
Any adverse event	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
感染症および寄生虫症	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
結膜炎	0	1 (25.0)	1 (16.7)	0	1 (16.7)
感染性腸炎	1 (50.0)	0	1 (16.7)	0	1 (16.7)
膿痂疹	0	1 (25.0)	1 (16.7)	0	1 (16.7)
インフルエンザ	0	1 (25.0)	1 (16.7)	0	1 (16.7)
上気道感染	0	1 (25.0)	1 (16.7)	0	1 (16.7)
傷害、中毒および処置合併症	0	2 (50.0)	2 (33.3)	0	2 (33.3)
眼瞼挫傷	0	1 (25.0)	1 (16.7)	0	1 (16.7)
手骨折	0	1 (25.0)	1 (16.7)	0	1 (16.7)
靭帯捻挫	0	1 (25.0)	1 (16.7)	0	1 (16.7)
皮膚および皮下組織障害	0	1 (25.0)	1 (16.7)	0	1 (16.7)
紫斑	0	1 (25.0)	1 (16.7)	0	1 (16.7)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.1.1.2_J

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
Any adverse event	17 (56.7)	23 (48.9)	12 (75.0)	52 (55.9)
No Reasonable Possibility	13 (43.3)	16 (34.0)	11 (68.8)	40 (43.0)
Reasonable Possibility	4 (13.3)	7 (14.9)	1 (6.3)	12 (12.9)
血液およびリンパ系障害	3 (10.0)	3 (6.4)	1 (6.3)	7 (7.5)
No Reasonable Possibility	3 (10.0)	3 (6.4)	1 (6.3)	7 (7.5)
貧血	3 (10.0)	3 (6.4)	1 (6.3)	7 (7.5)
No Reasonable Possibility	3 (10.0)	3 (6.4)	1 (6.3)	7 (7.5)
血小板増加症	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
心臓障害	1 (3.3)	0	0	1 (1.1)
Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
心膜炎	1 (3.3)	0	0	1 (1.1)
Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
内分泌障害	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
甲状腺腫	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
眼障害	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
角膜炎	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
胃腸障害	6 (20.0)	9 (19.1)	5 (31.3)	20 (21.5)
No Reasonable Possibility	6 (20.0)	6 (12.8)	4 (25.0)	16 (17.2)
Reasonable Possibility	0	3 (6.4)	1 (6.3)	4 (4.3)
腹痛	0	2 (4.3)	2 (12.5)	4 (4.3)
No Reasonable Possibility	0	2 (4.3)	2 (12.5)	4 (4.3)
上腹部痛	1 (3.3)	2 (4.3)	0	3 (3.2)
No Reasonable Possibility	1 (3.3)	2 (4.3)	0	3 (3.2)
潰瘍性大腸炎	4 (13.3)	2 (4.3)	1 (6.3)	7 (7.5)
No Reasonable Possibility	4 (13.3)	2 (4.3)	0	6 (6.5)
Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
便秘	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
下痢	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
胃腸障害 (Cont.)				
血性下痢	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
小腸炎	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
鼓腸	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
排便回数増加	0	1 (2.1)	0	1 (1.1)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
胃食道逆流性疾患	0	1 (2.1)	1 (6.3)	2 (2.2)
No Reasonable Possibility	0	1 (2.1)	1 (6.3)	2 (2.2)
血便排泄	0	2 (4.3)	0	2 (2.2)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
悪心	0	3 (6.4)	1 (6.3)	4 (4.3)
No Reasonable Possibility	0	2 (4.3)	1 (6.3)	3 (3.2)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
膵炎	0	1 (2.1)	0	1 (1.1)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
胃腸障害 (Cont.)				
嘔吐	0	1 (2.1)	1 (6.3)	2 (2.2)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
一般・全身障害および投与部位の状態	3 (10.0)	6 (12.8)	0	9 (9.7)
No Reasonable Possibility	3 (10.0)	3 (6.4)	0	6 (6.5)
Reasonable Possibility	0	3 (6.4)	0	3 (3.2)
腋窩痛	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
胸痛	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
疲労	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
注射部位疼痛	0	1 (2.1)	0	1 (1.1)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
注射部位蕁麻疹	0	1 (2.1)	0	1 (1.1)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
末梢腫脹	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
発熱	2 (6.7)	1 (2.1)	0	3 (3.2)
No Reasonable Possibility	2 (6.7)	0	0	2 (2.2)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
肝胆道系障害	1 (3.3)	0	0	1 (1.1)
Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
高ビリルビン血症	1 (3.3)	0	0	1 (1.1)
Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
感染症および寄生虫症	6 (20.0)	8 (17.0)	6 (37.5)	20 (21.5)
No Reasonable Possibility	6 (20.0)	8 (17.0)	5 (31.3)	19 (20.4)
Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
気管支炎	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
せつ	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
サルモネラ菌性胃腸炎	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
上咽頭炎	2 (6.7)	2 (4.3)	1 (6.3)	5 (5.4)
No Reasonable Possibility	2 (6.7)	2 (4.3)	1 (6.3)	5 (5.4)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
感染症および寄生虫症 (Cont.)				
口腔ヘルペス	1 (3.3)	2 (4.3)	0	3 (3.2)
No Reasonable Possibility	1 (3.3)	2 (4.3)	0	3 (3.2)
咽頭炎	2 (6.7)	1 (2.1)	1 (6.3)	4 (4.3)
No Reasonable Possibility	2 (6.7)	1 (2.1)	1 (6.3)	4 (4.3)
レンサ球菌感染	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
上気道感染	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
尿路感染	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
水痘	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
ウイルス感染	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
ウイルス性上気道感染	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
感染症および寄生虫症 (Cont.)				
外陰膣真菌感染	0	0	1 (6.3)	1 (1.1)
Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
傷害、中毒および処置合併症	4 (13.3)	2 (4.3)	0	6 (6.5)
No Reasonable Possibility	4 (13.3)	2 (4.3)	0	6 (6.5)
節足動物咬傷	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
転倒	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
注入に伴う反応	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
靭帯捻挫	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
処置による疼痛	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
手首関節骨折	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
臨床検査	2 (6.7)	2 (4.3)	1 (6.3)	5 (5.4)
No Reasonable Possibility	2 (6.7)	1 (2.1)	1 (6.3)	4 (4.3)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
血圧上昇	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
C－反応性蛋白増加	0	1 (2.1)	0	1 (1.1)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
ヘモグロビン減少	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
肝酵素上昇	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
体重減少	1 (3.3)	1 (2.1)	0	2 (2.2)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
筋骨格系および結合組織障害	2 (6.7)	2 (4.3)	1 (6.3)	5 (5.4)
No Reasonable Possibility	1 (3.3)	2 (4.3)	1 (6.3)	4 (4.3)
Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
関節痛	1 (3.3)	0	1 (6.3)	2 (2.2)
No Reasonable Possibility	1 (3.3)	0	1 (6.3)	2 (2.2)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
筋骨格系および結合組織障害 (Cont.)				
背部痛	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
靭帯障害	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
四肢痛	1 (3.3)	0	0	1 (1.1)
Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
神経系障害	5 (16.7)	5 (10.6)	4 (25.0)	14 (15.1)
No Reasonable Possibility	3 (10.0)	3 (6.4)	4 (25.0)	10 (10.8)
Reasonable Possibility	2 (6.7)	2 (4.3)	0	4 (4.3)
頭痛	4 (13.3)	5 (10.6)	4 (25.0)	13 (14.0)
No Reasonable Possibility	3 (10.0)	3 (6.4)	4 (25.0)	10 (10.8)
Reasonable Possibility	1 (3.3)	2 (4.3)	0	3 (3.2)
意識消失	1 (3.3)	0	0	1 (1.1)
Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
片頭痛	1 (3.3)	0	0	1 (1.1)
Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
錯感覚	1 (3.3)	0	0	1 (1.1)
Reasonable Possibility	1 (3.3)	0	0	1 (1.1)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
神経系障害 (Cont.)				
振戦	0	1 (2.1)	1 (6.3)	2 (2.2)
No Reasonable Possibility	0	1 (2.1)	1 (6.3)	2 (2.2)
腎および尿路障害	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
糖尿	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)
生殖系および乳房障害	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
乳房痛	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
呼吸器、胸郭および縦隔障害	1 (3.3)	3 (6.4)	3 (18.8)	7 (7.5)
No Reasonable Possibility	1 (3.3)	3 (6.4)	3 (18.8)	7 (7.5)
咳嗽	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)
鼻閉	0	1 (2.1)	0	1 (1.1)
No Reasonable Possibility	0	1 (2.1)	0	1 (1.1)

表 7. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
口腔咽頭痛	1 (3.3)	1 (2.1)	2 (12.5)	4 (4.3)
No Reasonable Possibility	1 (3.3)	1 (2.1)	2 (12.5)	4 (4.3)
鼻漏	0	1 (2.1)	1 (6.3)	2 (2.2)
No Reasonable Possibility	0	1 (2.1)	1 (6.3)	2 (2.2)
皮膚および皮下組織障害	1 (3.3)	0	1 (6.3)	2 (2.2)
No Reasonable Possibility	1 (3.3)	0	1 (6.3)	2 (2.2)
結節性紅斑	1 (3.3)	0	0	1 (1.1)
No Reasonable Possibility	1 (3.3)	0	0	1 (1.1)
発疹	0	0	1 (6.3)	1 (1.1)
No Reasonable Possibility	0	0	1 (6.3)	1 (1.1)

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.1

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	19 (59.4)	27 (52.9)	14 (77.8)	60 (59.4)
No Reasonable Possibility	14 (43.8)	19 (37.3)	12 (66.7)	45 (44.6)
Reasonable Possibility	5 (15.6)	8 (15.7)	2 (11.1)	15 (14.9)
血液およびリンパ系障害	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
No Reasonable Possibility	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
貧血	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
No Reasonable Possibility	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
血小板増加症	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
心臓障害	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
心膜炎	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
内分泌障害	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
甲状腺腫	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
眼障害	1 (3.1)	1 (2.0)	0	2 (2.0)
No Reasonable Possibility	1 (3.1)	1 (2.0)	0	2 (2.0)
眼瞼炎	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
角膜炎	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
胃腸障害	6 (18.8)	9 (17.6)	5 (27.8)	20 (19.8)
No Reasonable Possibility	6 (18.8)	6 (11.8)	4 (22.2)	16 (15.8)
Reasonable Possibility	0	3 (5.9)	1 (5.6)	4 (4.0)
腹痛	0	2 (3.9)	2 (11.1)	4 (4.0)
No Reasonable Possibility	0	2 (3.9)	2 (11.1)	4 (4.0)
上腹部痛	1 (3.1)	2 (3.9)	0	3 (3.0)
No Reasonable Possibility	1 (3.1)	2 (3.9)	0	3 (3.0)
潰瘍性大腸炎	4 (12.5)	2 (3.9)	1 (5.6)	7 (6.9)
No Reasonable Possibility	4 (12.5)	2 (3.9)	0	6 (5.9)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
便秘	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
胃腸障害 (Cont.)				
下痢	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
血性下痢	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
小腸炎	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
鼓腸	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
排便回数増加	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
胃食道逆流性疾患	0	1 (2.0)	1 (5.6)	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	1 (5.6)	2 (2.0)
血便排泄	0	2 (3.9)	0	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
悪心	0	3 (5.9)	1 (5.6)	4 (4.0)
No Reasonable Possibility	0	2 (3.9)	1 (5.6)	3 (3.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
胃腸障害 (Cont.)				
膵炎	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
嘔吐	0	1 (2.0)	1 (5.6)	2 (2.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
一般・全身障害および投与部位の状態	5 (15.6)	7 (13.7)	1 (5.6)	13 (12.9)
No Reasonable Possibility	4 (12.5)	3 (5.9)	1 (5.6)	8 (7.9)
Reasonable Possibility	1 (3.1)	4 (7.8)	0	5 (5.0)
腋窩痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
胸痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
疲労	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
異常感	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
注射部位紅斑	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
注射部位疼痛	1 (3.1)	1 (2.0)	0	2 (2.0)
Reasonable Possibility	1 (3.1)	1 (2.0)	0	2 (2.0)
注射部位蕁麻疹	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
末梢腫脹	1 (3.1)	0	1 (5.6)	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	1 (5.6)	2 (2.0)
発熱	2 (6.3)	1 (2.0)	0	3 (3.0)
No Reasonable Possibility	2 (6.3)	0	0	2 (2.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
肝胆道系障害	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
高ビリルビン血症	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
感染症および寄生虫症	6 (18.8)	11 (21.6)	6 (33.3)	23 (22.8)
No Reasonable Possibility	6 (18.8)	11 (21.6)	5 (27.8)	22 (21.8)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
気管支炎	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
感染症および寄生虫症 (Cont.)				
せつ	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
サルモネラ菌性胃腸炎	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
上咽頭炎	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
No Reasonable Possibility	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
口腔ヘルペス	1 (3.1)	2 (3.9)	0	3 (3.0)
No Reasonable Possibility	1 (3.1)	2 (3.9)	0	3 (3.0)
外耳炎	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
咽頭炎	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
No Reasonable Possibility	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
レンサ球菌感染	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
上気道感染	0	3 (5.9)	0	3 (3.0)
No Reasonable Possibility	0	3 (5.9)	0	3 (3.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
感染症および寄生虫症 (Cont.)				
尿路感染	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
水痘	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
ウイルス感染	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
ウイルス性上気道感染	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
外陰腟真菌感染	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
傷害、中毒および処置合併症	4 (12.5)	2 (3.9)	0	6 (5.9)
No Reasonable Possibility	4 (12.5)	2 (3.9)	0	6 (5.9)
節足動物咬傷	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
転倒	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
傷害、中毒および処置合併症 (Cont.)				
注入に伴う反応	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
靭帯捻挫	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
処置による疼痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
手首関節骨折	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
臨床検査	2 (6.3)	2 (3.9)	2 (11.1)	6 (5.9)
No Reasonable Possibility	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
Reasonable Possibility	0	1 (2.0)	1 (5.6)	2 (2.0)
血圧上昇	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
C－反応性蛋白増加	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
ヘモグロビン減少	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
臨床検査 (Cont.)				
肝酵素上昇	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
単球数減少	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
好中球数減少	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
体重減少	1 (3.1)	1 (2.0)	0	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
白血球数減少	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
筋骨格系および結合組織障害	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
No Reasonable Possibility	1 (3.1)	2 (3.9)	1 (5.6)	4 (4.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
関節痛	1 (3.1)	0	1 (5.6)	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	1 (5.6)	2 (2.0)
背部痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
筋骨格系および結合組織障害 (Cont.)				
靱帯障害	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
四肢痛	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
神経系障害	6 (18.8)	5 (9.8)	4 (22.2)	15 (14.9)
No Reasonable Possibility	4 (12.5)	3 (5.9)	4 (22.2)	11 (10.9)
Reasonable Possibility	2 (6.3)	2 (3.9)	0	4 (4.0)
頭痛	5 (15.6)	5 (9.8)	4 (22.2)	14 (13.9)
No Reasonable Possibility	4 (12.5)	3 (5.9)	4 (22.2)	11 (10.9)
Reasonable Possibility	1 (3.1)	2 (3.9)	0	3 (3.0)
意識消失	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
片頭痛	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
錯感覚	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
振戦	0	1 (2.0)	1 (5.6)	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	1 (5.6)	2 (2.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
腎および尿路障害	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
糖尿	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
生殖系および乳房障害	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
乳房痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
呼吸器、胸郭および縦隔障害	1 (3.1)	3 (5.9)	3 (16.7)	7 (6.9)
No Reasonable Possibility	1 (3.1)	3 (5.9)	3 (16.7)	7 (6.9)
咳嗽	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
鼻閉	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
口腔咽頭痛	1 (3.1)	1 (2.0)	2 (11.1)	4 (4.0)
No Reasonable Possibility	1 (3.1)	1 (2.0)	2 (11.1)	4 (4.0)

表 8. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
鼻漏	0	1 (2.0)	1 (5.6)	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	1 (5.6)	2 (2.0)
皮膚および皮下組織障害	1 (3.1)	0	1 (5.6)	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	1 (5.6)	2 (2.0)
結節性紅斑	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
発疹	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.1_A

表 9. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
Any adverse event	2 (100)	4 (100)	2 (100)	8 (100)
No Reasonable Possibility	1 (50.0)	3 (75.0)	1 (50.0)	5 (62.5)
Reasonable Possibility	1 (50.0)	1 (25.0)	1 (50.0)	3 (37.5)
眼障害	0	1 (25.0)	0	1 (12.5)
No Reasonable Possibility	0	1 (25.0)	0	1 (12.5)
眼瞼炎	0	1 (25.0)	0	1 (12.5)
No Reasonable Possibility	0	1 (25.0)	0	1 (12.5)
一般・全身障害および投与部位の状態	2 (100)	1 (25.0)	1 (50.0)	4 (50.0)
No Reasonable Possibility	1 (50.0)	0	1 (50.0)	2 (25.0)
Reasonable Possibility	1 (50.0)	1 (25.0)	0	2 (25.0)
異常感	1 (50.0)	0	0	1 (12.5)
No Reasonable Possibility	1 (50.0)	0	0	1 (12.5)
注射部位紅斑	0	1 (25.0)	0	1 (12.5)
Reasonable Possibility	0	1 (25.0)	0	1 (12.5)
注射部位疼痛	1 (50.0)	0	0	1 (12.5)
Reasonable Possibility	1 (50.0)	0	0	1 (12.5)
末梢腫脹	0	0	1 (50.0)	1 (12.5)
No Reasonable Possibility	0	0	1 (50.0)	1 (12.5)

表 9. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（日本人安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
感染症および寄生虫症	0	3 (75.0)	0	3 (37.5)
No Reasonable Possibility	0	3 (75.0)	0	3 (37.5)
外耳炎	0	1 (25.0)	0	1 (12.5)
No Reasonable Possibility	0	1 (25.0)	0	1 (12.5)
上気道感染	0	2 (50.0)	0	2 (25.0)
No Reasonable Possibility	0	2 (50.0)	0	2 (25.0)
臨床検査	0	0	1 (50.0)	1 (12.5)
Reasonable Possibility	0	0	1 (50.0)	1 (12.5)
単球数減少	0	0	1 (50.0)	1 (12.5)
Reasonable Possibility	0	0	1 (50.0)	1 (12.5)
好中球数減少	0	0	1 (50.0)	1 (12.5)
Reasonable Possibility	0	0	1 (50.0)	1 (12.5)
白血球数減少	0	0	1 (50.0)	1 (12.5)
Reasonable Possibility	0	0	1 (50.0)	1 (12.5)
神経系障害	1 (50.0)	0	0	1 (12.5)
No Reasonable Possibility	1 (50.0)	0	0	1 (12.5)

表 9. 導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（日本人安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
神経系障害 (Cont.)				
頭痛	1 (50.0)	0	0	1 (12.5)
No Reasonable Possibility	1 (50.0)	0	0	1 (12.5)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.1_J

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
Any adverse event	20 (64.5)	22 (68.8)	42 (66.7)	10 (83.3)	52 (69.3)
No Reasonable Possibility	12 (38.7)	12 (37.5)	24 (38.1)	5 (41.7)	29 (38.7)
Reasonable Possibility	8 (25.8)	10 (31.3)	18 (28.6)	5 (41.7)	23 (30.7)
血液およびリンパ系障害	4 (12.9)	1 (3.1)	5 (7.9)	2 (16.7)	7 (9.3)
No Reasonable Possibility	3 (9.7)	1 (3.1)	4 (6.3)	0	4 (5.3)
Reasonable Possibility	1 (3.2)	0	1 (1.6)	2 (16.7)	3 (4.0)
貧血	3 (9.7)	1 (3.1)	4 (6.3)	1 (8.3)	5 (6.7)
No Reasonable Possibility	2 (6.5)	1 (3.1)	3 (4.8)	0	3 (4.0)
Reasonable Possibility	1 (3.2)	0	1 (1.6)	1 (8.3)	2 (2.7)
リンパ節症	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
好中球減少症	0	0	0	1 (8.3)	1 (1.3)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
耳および迷路障害	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
耳痛	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
眼障害	0	0	0	1 (8.3)	1 (1.3)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
眼障害 (Cont.)					
非感染性結膜炎	0	0	0	1 (8.3)	1 (1.3)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
胃腸障害	9 (29.0)	10 (31.3)	19 (30.2)	3 (25.0)	22 (29.3)
No Reasonable Possibility	7 (22.6)	7 (21.9)	14 (22.2)	3 (25.0)	17 (22.7)
Reasonable Possibility	2 (6.5)	3 (9.4)	5 (7.9)	0	5 (6.7)
腹痛	1 (3.2)	1 (3.1)	2 (3.2)	1 (8.3)	3 (4.0)
No Reasonable Possibility	1 (3.2)	1 (3.1)	2 (3.2)	1 (8.3)	3 (4.0)
上腹部痛	0	2 (6.3)	2 (3.2)	0	2 (2.7)
No Reasonable Possibility	0	2 (6.3)	2 (3.2)	0	2 (2.7)
アフタ性潰瘍	1 (3.2)	0	1 (1.6)	0	1 (1.3)
Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
潰瘍性大腸炎	6 (19.4)	4 (12.5)	10 (15.9)	2 (16.7)	12 (16.0)
No Reasonable Possibility	5 (16.1)	2 (6.3)	7 (11.1)	2 (16.7)	9 (12.0)
Reasonable Possibility	1 (3.2)	2 (6.3)	3 (4.8)	0	3 (4.0)
便秘	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
下痢	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
胃腸障害 (Cont.)					
消化不良	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
小腸炎	2 (6.5)	1 (3.1)	3 (4.8)	0	3 (4.0)
No Reasonable Possibility	2 (6.5)	0	2 (3.2)	0	2 (2.7)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
胃食道逆流性疾患	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
一般・全身障害および投与部位の状態	5 (16.1)	3 (9.4)	8 (12.7)	1 (8.3)	9 (12.0)
No Reasonable Possibility	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
Reasonable Possibility	4 (12.9)	2 (6.3)	6 (9.5)	1 (8.3)	7 (9.3)
胸痛	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
疲労	2 (6.5)	0	2 (3.2)	0	2 (2.7)
Reasonable Possibility	2 (6.5)	0	2 (3.2)	0	2 (2.7)
炎症	0	0	0	1 (8.3)	1 (1.3)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
注射部位紅斑	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
注射部位炎症	1 (3.2)	0	1 (1.6)	0	1 (1.3)
Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
注射部位浮腫	1 (3.2)	0	1 (1.6)	0	1 (1.3)
Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
注射部位疼痛	1 (3.2)	0	1 (1.6)	0	1 (1.3)
Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
注射部位そう痒感	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
注射部位腫脹	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
注射部位蕁麻疹	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
倦怠感	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
発熱	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
免疫系障害	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
薬物過敏症	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
感染症および寄生虫症	10 (32.3)	13 (40.6)	23 (36.5)	5 (41.7)	28 (37.3)
No Reasonable Possibility	10 (32.3)	12 (37.5)	22 (34.9)	5 (41.7)	27 (36.0)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
気管支炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
胃腸炎	2 (6.5)	0	2 (3.2)	1 (8.3)	3 (4.0)
No Reasonable Possibility	2 (6.5)	0	2 (3.2)	1 (8.3)	3 (4.0)
感染性嚢腫	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
インフルエンザ	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
喉頭炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
感染症および寄生虫症 (Cont.)					
無菌性髄膜炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
上咽頭炎	3 (9.7)	4 (12.5)	7 (11.1)	1 (8.3)	8 (10.7)
No Reasonable Possibility	3 (9.7)	4 (12.5)	7 (11.1)	1 (8.3)	8 (10.7)
口腔ヘルペス	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
中耳炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
咽頭炎	2 (6.5)	2 (6.3)	4 (6.3)	1 (8.3)	5 (6.7)
No Reasonable Possibility	2 (6.5)	2 (6.3)	4 (6.3)	1 (8.3)	5 (6.7)
気道感染	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
ウイルス性気道感染	0	0	0	1 (8.3)	1 (1.3)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
鼻炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
感染症および寄生虫症 (Cont.)					
癜風	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
歯膿瘍	0	0	0	1 (8.3)	1 (1.3)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
気管炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
上気道感染	2 (6.5)	3 (9.4)	5 (7.9)	2 (16.7)	7 (9.3)
No Reasonable Possibility	2 (6.5)	3 (9.4)	5 (7.9)	2 (16.7)	7 (9.3)
尿路感染	1 (3.2)	2 (6.3)	3 (4.8)	0	3 (4.0)
No Reasonable Possibility	1 (3.2)	2 (6.3)	3 (4.8)	0	3 (4.0)
水痘	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
傷害、中毒および処置合併症	0	1 (3.1)	1 (1.6)	1 (8.3)	2 (2.7)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	1 (8.3)	2 (2.7)
手骨折	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
傷害、中毒および処置合併症 (Cont.)					
関節損傷	0	0	0	1 (8.3)	1 (1.3)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
臨床検査	5 (16.1)	3 (9.4)	8 (12.7)	0	8 (10.7)
No Reasonable Possibility	4 (12.9)	1 (3.1)	5 (7.9)	0	5 (6.7)
Reasonable Possibility	1 (3.2)	2 (6.3)	3 (4.8)	0	3 (4.0)
血中ビリルビン増加	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
血中カルシウム減少	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
血中ナトリウム減少	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
骨密度減少	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
C一反応性蛋白増加	3 (9.7)	0	3 (4.8)	0	3 (4.0)
No Reasonable Possibility	2 (6.5)	0	2 (3.2)	0	2 (2.7)
Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
好酸球数増加	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
臨床検査 (Cont.)					
リンパ節触知	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
結核菌群検査陽性	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
好中球数減少	1 (3.2)	0	1 (1.6)	0	1 (1.3)
Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
白血球数減少	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
筋骨格系および結合組織障害	1 (3.2)	2 (6.3)	3 (4.8)	1 (8.3)	4 (5.3)
No Reasonable Possibility	1 (3.2)	1 (3.1)	2 (3.2)	1 (8.3)	3 (4.0)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
関節痛	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
背部痛	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
No Reasonable Possibility	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
筋骨格痛	0	0	0	1 (8.3)	1 (1.3)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
神経系障害	6 (19.4)	3 (9.4)	9 (14.3)	2 (16.7)	11 (14.7)
No Reasonable Possibility	4 (12.9)	2 (6.3)	6 (9.5)	1 (8.3)	7 (9.3)
Reasonable Possibility	2 (6.5)	1 (3.1)	3 (4.8)	1 (8.3)	4 (5.3)
頭痛	6 (19.4)	2 (6.3)	8 (12.7)	2 (16.7)	10 (13.3)
No Reasonable Possibility	4 (12.9)	2 (6.3)	6 (9.5)	1 (8.3)	7 (9.3)
Reasonable Possibility	2 (6.5)	0	2 (3.2)	1 (8.3)	3 (4.0)
感覚鈍麻	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
錯感覚	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
精神障害	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
No Reasonable Possibility	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
うつ病	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
No Reasonable Possibility	1 (3.2)	1 (3.1)	2 (3.2)	0	2 (2.7)
生殖系および乳房障害	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
月経困難症	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
呼吸器、胸郭および縦隔障害	4 (12.9)	5 (15.6)	9 (14.3)	3 (25.0)	12 (16.0)
No Reasonable Possibility	4 (12.9)	5 (15.6)	9 (14.3)	3 (25.0)	12 (16.0)
喘息	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
咳嗽	0	2 (6.3)	2 (3.2)	0	2 (2.7)
No Reasonable Possibility	0	2 (6.3)	2 (3.2)	0	2 (2.7)
鼻出血	0	0	0	2 (16.7)	2 (2.7)
No Reasonable Possibility	0	0	0	2 (16.7)	2 (2.7)
鼻浮腫	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
口腔咽頭痛	2 (6.5)	1 (3.1)	3 (4.8)	0	3 (4.0)
No Reasonable Possibility	2 (6.5)	1 (3.1)	3 (4.8)	0	3 (4.0)
アレルギー性鼻炎	0	2 (6.3)	2 (3.2)	0	2 (2.7)
No Reasonable Possibility	0	2 (6.3)	2 (3.2)	0	2 (2.7)
鼻漏	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
喘鳴	0	0	0	1 (8.3)	1 (1.3)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
皮膚および皮下組織障害	1 (3.2)	6 (18.8)	7 (11.1)	3 (25.0)	10 (13.3)
No Reasonable Possibility	1 (3.2)	2 (6.3)	3 (4.8)	1 (8.3)	4 (5.3)
Reasonable Possibility	0	4 (12.5)	4 (6.3)	2 (16.7)	6 (8.0)
脱毛症	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
皮膚炎	0	1 (3.1)	1 (1.6)	1 (8.3)	2 (2.7)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
紅斑	0	1 (3.1)	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
結節性紅斑	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
逆むけ	0	0	0	1 (8.3)	1 (1.3)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
乾癬	0	0	0	1 (8.3)	1 (1.3)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)

表 10. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
皮膚および皮下組織障害 (Cont.)					
発疹	1 (3.2)	2 (6.3)	3 (4.8)	0	3 (4.0)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
Reasonable Possibility	0	2 (6.3)	2 (3.2)	0	2 (2.7)
痂皮	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)
脂漏	1 (3.2)	0	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	1 (3.2)	0	1 (1.6)	0	1 (1.3)
皮膚病変	0	1 (3.1)	1 (1.6)	0	1 (1.3)
No Reasonable Possibility	0	1 (3.1)	1 (1.6)	0	1 (1.3)

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.2

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	21 (63.6)	26 (72.2)	47 (68.1)	10 (83.3)	57 (70.4)
No Reasonable Possibility	13 (39.4)	15 (41.7)	28 (40.6)	5 (41.7)	33 (40.7)
Reasonable Possibility	8 (24.2)	11 (30.6)	19 (27.5)	5 (41.7)	24 (29.6)
血液およびリンパ系障害	4 (12.1)	1 (2.8)	5 (7.2)	2 (16.7)	7 (8.6)
No Reasonable Possibility	3 (9.1)	1 (2.8)	4 (5.8)	0	4 (4.9)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	2 (16.7)	3 (3.7)
貧血	3 (9.1)	1 (2.8)	4 (5.8)	1 (8.3)	5 (6.2)
No Reasonable Possibility	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	1 (8.3)	2 (2.5)
リンパ節症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
好中球減少症	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
耳および迷路障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
耳痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
眼障害	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
眼障害 (Cont.)					
非感染性結膜炎	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
胃腸障害	9 (27.3)	10 (27.8)	19 (27.5)	3 (25.0)	22 (27.2)
No Reasonable Possibility	7 (21.2)	7 (19.4)	14 (20.3)	3 (25.0)	17 (21.0)
Reasonable Possibility	2 (6.1)	3 (8.3)	5 (7.2)	0	5 (6.2)
腹痛	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
上腹部痛	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
アフタ性潰瘍	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
潰瘍性大腸炎	6 (18.2)	4 (11.1)	10 (14.5)	2 (16.7)	12 (14.8)
No Reasonable Possibility	5 (15.2)	2 (5.6)	7 (10.1)	2 (16.7)	9 (11.1)
Reasonable Possibility	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
便秘	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
下痢	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
胃腸障害 (Cont.)					
消化不良	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
小腸炎	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
胃食道逆流性疾患	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
一般・全身障害および投与部位の状態	5 (15.2)	3 (8.3)	8 (11.6)	1 (8.3)	9 (11.1)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
Reasonable Possibility	4 (12.1)	2 (5.6)	6 (8.7)	1 (8.3)	7 (8.6)
胸痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
疲労	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Reasonable Possibility	2 (6.1)	0	2 (2.9)	0	2 (2.5)
炎症	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
注射部位紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
注射部位炎症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位疼痛	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位そう痒感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位腫脹	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位蕁麻疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
倦怠感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発熱	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
免疫系障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
薬物過敏症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染症および寄生虫症	11 (33.3)	17 (47.2)	28 (40.6)	5 (41.7)	33 (40.7)
No Reasonable Possibility	11 (33.3)	15 (41.7)	26 (37.7)	5 (41.7)	31 (38.3)
Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
気管支炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
結膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染性腸炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
胃腸炎	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
No Reasonable Possibility	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
膿痂疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
感染性嚢腫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
インフルエンザ	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
喉頭炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
無菌性髄膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
上咽頭炎	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)	8 (9.9)
No Reasonable Possibility	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)	8 (9.9)
口腔ヘルペス	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
中耳炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
咽頭炎	2 (6.1)	2 (5.6)	4 (5.8)	1 (8.3)	5 (6.2)
No Reasonable Possibility	2 (6.1)	2 (5.6)	4 (5.8)	1 (8.3)	5 (6.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
気道感染	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
ウイルス性気道感染	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
鼻炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
癜風	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
歯膿瘍	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
気管炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
上気道感染	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)	8 (9.9)
No Reasonable Possibility	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)	8 (9.9)
尿路感染	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
水痘	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
傷害、中毒および処置合併症	0	3 (8.3)	3 (4.3)	1 (8.3)	4 (4.9)
No Reasonable Possibility	0	3 (8.3)	3 (4.3)	1 (8.3)	4 (4.9)
眼瞼挫傷	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
手骨折	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
関節損傷	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
靭帯捻挫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
臨床検査	5 (15.2)	3 (8.3)	8 (11.6)	0	8 (9.9)
No Reasonable Possibility	4 (12.1)	1 (2.8)	5 (7.2)	0	5 (6.2)
Reasonable Possibility	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
血中ビリルビン増加	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
臨床検査 (Cont.)					
血中カルシウム減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
血中ナトリウム減少	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
骨密度減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
C－反応性蛋白増加	3 (9.1)	0	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
好酸球数増加	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
リンパ節触知	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
結核菌群検査陽性	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
好中球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
臨床検査 (Cont.)					
白血球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
筋骨格系および結合組織障害	1 (3.0)	2 (5.6)	3 (4.3)	1 (8.3)	4 (4.9)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
関節痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
背部痛	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
筋骨格痛	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
神経系障害	6 (18.2)	3 (8.3)	9 (13.0)	2 (16.7)	11 (13.6)
No Reasonable Possibility	4 (12.1)	2 (5.6)	6 (8.7)	1 (8.3)	7 (8.6)
Reasonable Possibility	2 (6.1)	1 (2.8)	3 (4.3)	1 (8.3)	4 (4.9)
頭痛	6 (18.2)	2 (5.6)	8 (11.6)	2 (16.7)	10 (12.3)
No Reasonable Possibility	4 (12.1)	2 (5.6)	6 (8.7)	1 (8.3)	7 (8.6)
Reasonable Possibility	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
感覚鈍麻	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
神経系障害 (Cont.)					
錯感覚	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
精神障害	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
うつ病	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
生殖系および乳房障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
月経困難症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
呼吸器、胸郭および縦隔障害	4 (12.1)	5 (13.9)	9 (13.0)	3 (25.0)	12 (14.8)
No Reasonable Possibility	4 (12.1)	5 (13.9)	9 (13.0)	3 (25.0)	12 (14.8)
喘息	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
咳嗽	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
鼻出血	0	0	0	2 (16.7)	2 (2.5)
No Reasonable Possibility	0	0	0	2 (16.7)	2 (2.5)
鼻浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
口腔咽頭痛	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
アレルギー性鼻炎	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
鼻漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
喘鳴	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
皮膚および皮下組織障害	1 (3.0)	7 (19.4)	8 (11.6)	3 (25.0)	11 (13.6)
No Reasonable Possibility	1 (3.0)	2 (5.6)	3 (4.3)	1 (8.3)	4 (4.9)
Reasonable Possibility	0	5 (13.9)	5 (7.2)	2 (16.7)	7 (8.6)
脱毛症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
皮膚および皮下組織障害 (Cont.)					
皮膚炎	0	1 (2.8)	1 (1.4)	1 (8.3)	2 (2.5)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
結節性紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
逆むけ	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
乾癬	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
紫斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発疹	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
痂皮	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 11. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
皮膚および皮下組織障害 (Cont.)					
脂漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
皮膚病変	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.2_A

表 12. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total-ADA (N=6) n (%)	M-PL (N=0) n (%)	Total (N=6) n (%)
Any adverse event	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
No Reasonable Possibility	1 (50.0)	3 (75.0)	4 (66.7)	0	4 (66.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
感染症および寄生虫症	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
No Reasonable Possibility	1 (50.0)	3 (75.0)	4 (66.7)	0	4 (66.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
結膜炎	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
感染性腸炎	1 (50.0)	0	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	1 (50.0)	0	1 (16.7)	0	1 (16.7)
膿痂疹	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
インフルエンザ	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
上気道感染	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
傷害、中毒および処置合併症	0	2 (50.0)	2 (33.3)	0	2 (33.3)
No Reasonable Possibility	0	2 (50.0)	2 (33.3)	0	2 (33.3)

表 12. 維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（日本人安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total-ADA (N=6) n (%)	M-PL (N=0) n (%)	Total (N=6) n (%)
傷害、中毒および処置合併症 (Cont.)					
眼瞼挫傷	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
手骨折	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
靭帯捻挫	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
皮膚および皮下組織障害	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
紫斑	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.2_J

重篤な有害事象の叙述

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHDOL-MSD-FREIND	1[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: ECZEMA	20[redacted]
ASTHMA/REACTIVE AIRWAY DISEASE: ASTHMA	20[redacted]
OTHER: HEADACHES	20[redacted]
Ulcerative colitis	20[redacted]
COGNITIVE, BEHAVIORAL OR PSYCHIATRIC DISORDER: ANXIETY	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHDOL	[redacted] / 1	[redacted] / 44	56
MSD	[redacted] / 57	[redacted] / 121	70
FREIND	[redacted] / 127	[redacted] / 219	106

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
VITAMINS NOS	1 DF (dosage form)	QD	Y-M: [redacted]
COLECALCIFEROL	2,000 IU (international unit(s))	QD	Y-M: [redacted]
PARACETAMOL	325 mg (milligram(s))	PRN	Y-M: [redacted]
BALSALAZIDE	2250 mg (milligram(s))	TID	Y-M: [redacted]
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: [redacted] / -92
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: [redacted] / -42
AMOXICILLIN	500 mg (milligram(s))	TID	Y-M: [redacted] / -15
FLEET	1 DF (dosage form)	OTHER: TWICE	Y-M: [redacted] / -6
LIDOCAINE	100 mg (milligram(s))	OTHER: ONCE	Y-M: [redacted] / -6
PROPOFOL	200 mg (milligram(s))	OTHER: ONCE	Y-M: [redacted] / -6

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
VITAMINS NOS	1 DF (dosage form)	QD	Y-M: [redacted]	ONGOING
COLECALCIFEROL	2,000 IU (international unit(s))	QD	Y-M: [redacted]	ONGOING
PARACETAMOL	325 mg (milligram(s))	PRN	Y-M: [redacted]	ONGOING
BALSALAZIDE	2250 mg (milligram(s))	TID	Y-M: [redacted]	ONGOING
AMOXICILLIN	500 mg (milligram(s))	BID	Y-M: [redacted] / 164	Y-M: [redacted] / 174
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: [redacted] / 203	Y-M: [redacted] / 209
LOPERAMIDE HYDROCHLORIDE	4 mg (milligram(s))	BID	Y-M: [redacted] / 208	Y-M: [redacted] / 244
PREDNISONE	30 mg (milligram(s))	BID	Y-M: [redacted] / 211	Y-M: [redacted] / 221
GLYCOPYRRONIUM BROMIDE	0.2 mg (milligram(s))	OTHER: ONCE	Y-M: [redacted] / 219	Y-M: [redacted] / 219

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
PROPOFOL	230 mg (milligram(s))	OTHER: ONCE	Y-M: 20[redacted] / 219	Y-M: 20[redacted] / 219
PREDNISONE	25 mg (milligram(s))	BID	Y-M: 20[redacted] / 222	Y-M: 20[redacted] / 223
VALGANCICLOVIR	900 mg (milligram(s))	BID	Y-M: 20[redacted] / 222	Y-M: 20[redacted] / 242
PREDNISONE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / 224	Y-M: 20[redacted] / 225
PREDNISONE	15 mg (milligram(s))	BID	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 227
PREDNISONE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 229
PREDNISONE	5 mg (milligram(s))	BID	Y-M: 20[redacted] / 230	Y-M: 20[redacted] / 231
PROPOFOL	250 mg (milligram(s))	OTHER: ONCE	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 243
DEXTROSE AND SODIUM CHLORIDE INJECTION	1000 mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 245
SODIUM CHLORIDE	1000 mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 245
FAMOTIDINE	20 mg (milligram(s))	OTHER: Q12H	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 250
LIDOCAINE	1 APPLICATION	PRN	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 250
METHYLPREDNISOLONE	25 mg (milligram(s))	OTHER: Q12H	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 250
MORPHINE	4 mg (milligram(s))	OTHER: PRN Q2H	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 250
PARACETAMOL	750 mg (milligram(s))	OTHER: PRN Q6H	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 250
VANCOMYCIN	125 mg (milligram(s))	QID	Y-M: 20[redacted] / 246	Y-M: 20[redacted] / 255
SACCHARATED IRON OXIDE	100 mL (millilitre(s))	QD	Y-M: 20[redacted] / 247	Y-M: 20[redacted] / 249
INFLIXIMAB	300 mg (milligram(s))	OTHER: WEEK 0, WEEK 2, WEEK 6	Y-M: 20[redacted] / 249	ONGOING
LORATADINE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / 249	ONGOING

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
METHYLPREDNISOLONE SODIUM SUCCINATE	40 mg (milligram(s))	OTHER: Q8WK	Y-M: 20[redacted] / 249	ONGOING
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 251	Y-M: 20[redacted] / 251
RANITIDINE	75 mg (milligram(s))	BID	Y-M: 20[redacted] / 251	Y-M: 20[redacted] / 253
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 252
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 253	Y-M: 20[redacted] / 253
PREDNISONE	60 mg (milligram(s))	QD	Y-M: 20[redacted] / 258	Y-M: 20[redacted] / 262
PREDNISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 263	Y-M: 20[redacted] / 267
INFLUENZA VACCINE	0.5 mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] / 266	Y-M: 20[redacted] / 266
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 268	Y-M: 20[redacted] / 272
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 273	Y-M: 20[redacted] / 279
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 280	Y-M: 20[redacted] / 286
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 287	Y-M: 20[redacted] / 295
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 296	ONGOING
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / 296	ONGOING

Event #1: Serious Adverse Event

Event Description	WORSENING ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 203
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 209): FECAL CALPROTECTIN: 366 [NOT REPORTED - 50] MCG/G; [redacted]20[redacted] (RX DAY 245): C-REACTIVE PROTEIN: 1.87 [NOT REPORTED - 5] MG/DL; [redacted]20[redacted] (RX DAY 249): C-REACTIVE PROTEIN: <0.29 [NOT REPORTED - 5] MG/DL

Microbiology

[redacted]20[redacted] (RX DAY 219): Other COLON BIOPSY CMV INFECTION: POSITIVE-COLON, SIGMOID AND RECTUM BIOPSIED AND POSITIVE FOR SUPERIMPOSED CMV INFECTION WITH LOW DENSITY OF CMV INFECTED CELLS; [redacted]20[redacted](RX DAY 245): Stool C. DIFFICILE: POSITIVE-RESULTS WERE POSITIVE FOR C. DIFFICILE

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CYTOMEGALOVIRUS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until

second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男児（米国）であり，重篤な有害事象の潰瘍性大腸炎悪化を発現した。関連する病歴は，潰瘍性大腸炎であった。被験者は非喫煙者及び非アルコール摂取者であった。
当該被験者は，最初の 7 週間は非盲検下でアダリムマブ導入療法期高用量に無作為に割り付けられ，20[redacted] 年[redacted] 月[redacted] 日に再度，盲検下でアダリムマブに無作為に割り付けられた。
20[redacted] 年[redacted] 月[redacted] 日，潰瘍性大腸炎悪化が発現した。
本事象発現前の 20[redacted] 年[redacted] 月[redacted] 日～20[redacted] 年[redacted] 月[redacted] 日に，非重篤な有害事象として潰瘍性大腸炎悪化の症状が認められていた。
入院前の 20[redacted] 年[redacted] 月[redacted] 日，結腸生検が実施された。
20[redacted] 年[redacted] 月[redacted] 日，血性及び非血性下痢の排便が増加したため（1 日最高 9 回），被験者は入院した。日中の便失禁等，夜間の排便，食欲減退及び体重減少の継続も報告された。ステロイドが静脈内投与された。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。
治療薬としてメチルプレドニゾロン，モルヒネ，アセトアミノフェン，ブドウ糖／塩化カリウム／塩化ナトリウム，塩化ナトリウム，Remicade（インフリキシマブ），インフリキシマブ，ラニチジン，Flagyl（メトロニダゾール），Imodium（ロペラミド塩酸塩），balsalazide，prednisone 及びファモチジンが投与された。

The patient's past medications include:

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

Causality for HUMIRA (Blinded)

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

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA (Blinded)

Event of WORSENING ULCERATIVE COLITIS

- Investigator: Cytomegalovirus

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] COLONIC BIOPSY: Colon, sigmoid and rectum biopsied and positive for superimposed cytomegalovirus (CMV) infection with low density of CMV infected cells.

[redacted] 20[redacted] CRP: 1.87 mg/dL

[redacted] 20[redacted] CRP: . <0.29 mg/dl

[redacted] 20[redacted] ELEVATED FECAL CALPROTECTIN: 366 mcg/g

[redacted] 20[redacted] HEMOGLOBIN: 10.9 G/DL

[redacted] 20[redacted] HEMOGLOBIN: 11.6 G/DL

[redacted] 20[redacted] RBC: 4.48 m/uL

[redacted] 20[redacted] STOOL CULTURE: results were positive for c. difficile (non serious)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
無菌性髄膜炎	X			

Treatment Group	Age at Study Start	Sex	Race
IHD-MHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
MIGRAINE HEADACHE: LONG STANDING HISTORY OF MIGRAINE HEADACHES	NOT REPORTED
EAR INFECTIONS/PRESSURE EQUALIZATION TUBES: MYRINGOTOMY	20[redacted]
TONSILLECTOMY/ADENOIDECTOMY: ADENOIDECTOMY	20[redacted]
EAR INFECTIONS/PRESSURE EQUALIZATION TUBES: MYRINGOTOMY	20[redacted]
EAR INFECTIONS/PRESSURE EQUALIZATION TUBES: MYRINGOTOMY	20[redacted]
Ulcerative colitis	20[redacted]
EAR INFECTIONS/PRESSURE EQUALIZATION TUBES: MIDDLE EAR INFECTION	20[redacted]
OTHER: MASTOIDITIS	20[redacted]
OTHER: SINUSITIS	20[redacted]
DRUG ALLERGIES/REACTIONS: HIVES SECONDARY TO REMICADE	20[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGIC REACTION TO METHOTREXATE	20[redacted]
COGNITIVE, BEHAVIORAL OR PSYCHIATRIC DISORDER: SUBJECT HAS INTERMITTENT AND LONG-STANDING ISSUES WITH ANXIETY; IS MEETING WITH PSYCHOLOGY DEPARTMENT HERE IN [redacted]	20[redacted]
DEPRESSION: HISTORY OF DEPRESSION, CURRENTLY IN REMISSION	20[redacted]
OTHER: IRREGULAR PERIODS	20[redacted]
OTHER: ELEVATED TRIGLYCERIDES	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted] / 1	[redacted] / 41	54
MHD	[redacted] / 57	[redacted] / 364	309

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
NORLESTRIN FE	1 TABLET	QD	Y-M: [redacted] / -37
NORTRIPTYLINE	20 mg (milligram(s))	QD	Y-M: [redacted] / -21
SUMATRIPTAN	50 mg (milligram(s))	PRN	Y-M: [redacted] / -21
FLEET	133 mL (millilitre(s))	OTHER: ONCE	Y-M: [redacted] / -14
PROPOFOL	230 mg (milligram(s))	OTHER: ONCE	Y-M: [redacted] / -14
AUGMENTIN	875 mg (milligram(s))	BID	Y-M: [redacted] / -6

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
NORLESTRIN FE	1 TABLET	QD	Y-M: [redacted] / -37	ONGOING
SUMATRIPTAN	50 mg (milligram(s))	PRN	Y-M: [redacted] / -21	ONGOING
CEFTRIAXONE	2 g (gram(s))	OTHER: ONCE	Y-M: [redacted] / 61	Y-M: [redacted] / 61
DIPHENHYDRAMINE HYDROCHLORIDE	12.5 mg (milligram(s))	OTHER: ONCE	Y-M: [redacted] / 61	Y-M: [redacted] / 61
KETOROLAC	30 mg (milligram(s))	OTHER: Q6H PRN	Y-M: [redacted] /	Y-M: [redacted] /

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
			61	61
MIDAZOLAM	1 mg (milligram(s))	OTHER: ONCE	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 61
PROCHLORPERAZINE MALEATE	10 mg (milligram(s))	OTHER: ONCE	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 61
SODIUM CHLORIDE	1000 mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 61
SODIUM CHLORIDE	500 mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 61
ACICLOVIR	600 mg (milligram(s))	OTHER: Q8H	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 62
VANCOMYCIN	1250 mg (milligram(s))	OTHER: Q8H	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 62
KETOROLAC	15 mg (milligram(s))	OTHER: Q6H PRN	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 64
HEPARIN	5000 UNITS	TID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 65
PARACETAMOL	1000 mg (milligram(s))	OTHER: Q6H PRN	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 66
GABAPENTIN	300 mg (milligram(s))	TID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 91
LORAZEPAM	0.5 mg (milligram(s))	PRN	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 91
ONDANSETRON	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 91
VICODIN	5-325 mg (milligram(s))	PRN	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 91
AMPICILLIN	2 g (gram(s))	OTHER: Q4H	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
CEFEPIME	2 g (gram(s))	OTHER: Q8H	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
CEFTRIAXONE	2 g (gram(s))	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
HYDROMORPHONE HYDROCHLORIDE	0.5 mg (milligram(s))	OTHER: ONCE	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
VALACICLOVIR HYDROCHLORIDE	1000 mg (milligram(s))	OTHER: Q8H	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 64
MORPHINE	4 mg (milligram(s))	OTHER: Q1H PRN	Y-M: 20[redacted] /	Y-M: 20[redacted] /

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
			62	65
ONDANSETRON	4 mg (milligram(s))	OTHER: Q8H PRN	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 65
OXYCOCET	2 TABLETS	OTHER: Q4H PRN	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 64
LORAZEPAM	0.5 mg (milligram(s))	OTHER: Q6H PRN	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 65
SODIUM CHLORIDE	75 ML/HR	OTHER: CONTINUOUS	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 65
OXYCODONE HYDROCHLORIDE	10 mg (milligram(s))	OTHER: Q4H PRN	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 66
GADODIAMIDE	12 mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 65
TRAMADOL HYDROCHLORIDE	50 mg (milligram(s))	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
COLOXYL WITH SENNA	1 TABLET	PRN	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 91
MACROGOL 3350	17 g (gram(s))	PRN	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 91

Event #1: Serious Adverse Event

Event Description	ASEPTIC MENINGITIS
Preferred term	無菌性髄膜炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 61
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 61): BLOOD CULTURES: NEGATIVE; URINE CULTURE: NEGATIVE; THROAT CULTURE: NO GROUP A BETA STREP; CEREBRAL SPINAL FLUID BACTERIAL CULTURE: NEGATIVE; HEAD CT: NORMAL UNENHANCED CT OF THE HEAD; LUMBAR PUNCTURE: 52 NUCLEATED CELLS, 48% PMN, 47% LYMPH, 38 PROTEIN AND 60 GLUCOSE.; [redacted]20[redacted] (RX DAY 65): BRAIN MRV: NORMAL INTRACRANIAL MR VENOGRAM; BRAIN MRI: NORMAL MRI OF THE BRAIN WITH INTRAVENOUS CONTRAST

AE Stopped Rx Day	67
Duration of AE	7 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

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女性（米国）であり，重篤な有害事象の無菌性髄膜炎を発現した。関連する病歴は，潰瘍性大腸炎（左側），乳様突起炎，中耳感染，副鼻腔炎及び長期にわたる片頭痛であった。被験者は非喫煙者であり，飲酒の習慣はなかった。
20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な有害事象である発熱が発現し，同日に自然回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，無菌性髄膜炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，無菌性髄膜炎は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，高度の頭痛及び発熱のため，被験者は救急治療室を受診し，その後地域の病院に入院した。被験者は無菌性髄膜炎と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬としてガバペンチン，Norco（酒石酸水素ヒドロコドン／アセトアミノフェン），Ativan（ロラゼパム），Zofran（オンダンセトロン塩酸塩水和物），Miralax，Senna-S，アセトアミノフェン，プロクロルペラジンマレイン酸塩，0.9%塩化ナトリウム，Ketorolac，ミダゾラム，セフトリアキソン，バンコマイシン，アシクロビル，アンピシリン，セフェピム，ヘパリン，Dilaudid（ヒドロモルフォン塩酸塩），モルヒネ，Valtrex（バラシクロビル塩酸塩），Percocet（アセトアミノフェン／オキシコドン塩酸塩），オキシコドン塩酸塩，Omniscan（ガドジアミド水和物）及び Ultram（トラマドール塩酸塩）が投与された。

The patient's past medications include:

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

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

Causality for HUMIRA (Blinded)

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1) Aseptic meningitis (10003458) (Meningitis aseptic (10027201)) [v.19.1] [10003458]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: No

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ASEPTIC MENINGITIS

- Investigator: N/A

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD CULTURES: negative

[redacted] 20[redacted] Brain MRI: Normal MRI of brain with IV contrast

[redacted] 20[redacted] Brain MRV: Normal intracranial MR venogram

[redacted] 20[redacted] CEREBRAL SPINAL FLUID BACTERIAL CULTURE: Negative

Unknown date Culture: Negative

[redacted] 20[redacted] ELECTROCARDIOGRAM: NORMAL

[redacted] 20[redacted] Flexible sigmoidoscopy: Rectum/sigmoid: 3, severe disease

[redacted] 20[redacted] Head CT: Normal unenhanced CT of head

[redacted] 20[redacted] Lumbar Puncture:

Puncture: 52 nucleated cells, 48% PMN, 47% Lymph, 38 protein and 60 glucose.

[redacted] 20[redacted] THROAT CULTURE: No group A beta strep

[redacted] 20[redacted] URINE CULTURE: Negative

[redacted] 20[redacted] WBC: 15.6 X10**9/L

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD-MSD	1[redacted]	MALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
OTHER: SEASONAL ALLERGIES	NOT REPORTED
OTHER: VITAMIN D DEFICIENCY	20[redacted]
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MSD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 120	77

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
COLECALCIFEROL	5000 IU (international unit(s))	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -294
OMEPRAZOLE	20 mg (milligram(s))	PRN	Y-M: 20[redacted] / -291
MESALAZINE	2000 mg (milligram(s))	BID	Y-M: 20[redacted] / -287
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -71
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / -15
IBUPROFEN	800 mg (milligram(s))	PRN	Y-M: 20[redacted] / -12
ENEMAS	UNK mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] / -10

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
COLECALCIFEROL	5000 IU (international unit(s))	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -294	ONGOING
OMEPRAZOLE	20 mg (milligram(s))	PRN	Y-M: 20[redacted] / -291	ONGOING
MESALAZINE	2000 mg (milligram(s))	BID	Y-M: 20[redacted] / -287	ONGOING
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / -15	ONGOING
IBUPROFEN	800 mg (milligram(s))	PRN	Y-M: 20[redacted] / -12	ONGOING
FERROUS FUMARATE	89 mg (milligram(s))	QD	Y-M: 20[redacted] / 98	ONGOING
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 122
PREDNISONE	35 mg (milligram(s))	QD	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 129
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 132
VICODIN	325 mg (milligram(s))	PRN	Y-M: 20[redacted] / 132	ONGOING
ADALIMUMAB	160 mg (milligram(s))	OTHER: ONCE TO START INDUCTION OF THERAPY	Y-M: 20[redacted] / 132	Y-M: 20[redacted] / 132

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
DIPHENHYDRAMINE	50 mg (milligram(s))	OTHER: Q6HRS	Y-M: 20[redacted]-[redacted] / 132	Y-M: 20[redacted]-[redacted] / 132
METHYLPREDNISOLONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 132	Y-M: 20[redacted]-[redacted] / 132
METHYLPREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 133	Y-M: 20[redacted]-[redacted] / 133
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 134	ONGOING

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 131 (11 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	138 (18 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	WORSENING ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and

Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男性（米国）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎）及び軟性 S 状結腸鏡（直腸は軽度，S 状結腸は高度）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。

被験者は高度の腹痛を有していた。20[redacted] 年 [redacted] 月 [redacted] 日，症状の再燃のため，被験者はクリニックを救急で受診した。被験者及び被験者の母親は，症状は有害事象が発現する約 2 ヵ月前に再発し，直近の 1 週間で急激に悪化したと報告した。腹痛は恒常的に認められていたが，経口摂取時に自然と悪化した。Tylenol（アセトアミノフェン）又は Motrin（イブプロフェン）により緩和しなかった。腹痛のため，被験者は夜間に目を覚ますことがあり，排便は有形軟便であった。入院する 1 週間前には血便が認められたが，その後はみられなかった。救急治療室では漸減した prednisone が処方されたが，症状は改善しなかった。発熱，悪心又は嘔吐は認められなかった。臨床検査が実施されたが検査結果に異常はなかった。腹痛に対して Norco（酒石酸水素ヒドロコドン／アセトアミノフェン）が投与され，メチルプレドニゾロンの投与が開始された。アダリムマブの投与も開始され，症状の再燃予防のため，ジフェンヒドラミン塩酸塩が投与された。翌日には若干の改善が認められ，経口摂取時の忍容性も改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は prednisone（経口投与）及び鎮痛剤（在宅用）を処方され，消化器科の医師による経過観察を受けるよう指示を受け，退院した。

治療薬としてメチルプレドニゾロン，hydrocodone／アセトアミノフェン，prednisone 及びジフェンヒドラミンが投与された。

The patient's past medications include:

PREDNISONE forULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ULCERATIVE COLITIS FLARE

- Investigator: Worsening ulcerative colitis

- AbbVie: The underlying disorder UC

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD	1[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: OBESITY	20[redacted]
OTHER: SLEEP APNEA	20[redacted]
OTHER: SNORING	20[redacted]
TONSILLECTOMY/ADENOIDECTOMY: TONSILLECTOMY AND ADENOIDECTOMY	20[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO PREDNISONE- CAUSES AGITATION	20[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO PREDNISONE- CAUSES INSOMNIA	20[redacted]
OTHER: ACNE	20[redacted]
OTHER: ETHMOIDITIS	20[redacted]
OTHER: PHARYNGITIS	20[redacted]
OTHER: BLOODY DIARRHEA	20[redacted]
OTHER: CONSTIPATION	20[redacted]
OTHER: PERIUMBILICAL ABDOMINAL PAIN	20[redacted]
OTHER: FLATULENCE	20[redacted]
OTHER: INTERMITTENT FEVERS	20[redacted]
OTHER: INTERMITTENT LOSS OF APPETITE	20[redacted]
OTHER: INTERMITTENT NAUSEA	20[redacted]
OTHER: KERATOSIS	20[redacted]
OTHER: ABDOMINAL DISTENTION	20[redacted]
OTHER: FATIGUE	20[redacted]
OTHER: GASTRITIS	20[redacted]
OTHER: INTERMITTENT EMESIS	20[redacted]
OTHER: INTERMITTENT NOCTURNAL DEFECATION	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: FAILURE OF STEROID INDEPENDENCE	20[redacted]
OTHER: INTERMITTENT HEADACHES	20[redacted]

Medical History	Onset Year
OTHER: WEIGHT LOSS	20[redacted]
PANCREATITIS: ACUTE PANCREATITIS SECONDARY TO ULCERATIVE COLITIS FLARE	20[redacted]
ANEMIA: ANEMIA	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BENZOYL PEROXIDE	1 APPLICATION	BID	Y-M: 20[redacted]
ERGOCALCIFEROL	1 TABLET	QD	Y-M: 20[redacted]-[redacted] / -163
FISH OIL	1 CAPSULE	QD	Y-M: 20[redacted]-[redacted] / -163
FOLIC ACID	1 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -163
MESALAZINE	1125 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -163
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -163
VSL#3	1 CAPSULE	BID	Y-M: 20[redacted]-[redacted] / -155
BUDESONIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted] / -105
METHYLPREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted] / -36
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted] / -32
FERROUS GLUCONATE	225 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -7
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -7

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SUCRALFATE	1 g (gram(s))	TID	Y-M: 20[redacted] / -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BENZOYL PEROXIDE	1 APPLICATION	BID	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	1 TABLET	QD	Y-M: 20[redacted] / -163	ONGOING
FISH OIL	1 CAPSULE	QD	Y-M: 20[redacted] / -163	ONGOING
FOLIC ACID	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -163	ONGOING
MESALAZINE	1125 mg (milligram(s))	BID	Y-M: 20[redacted] / -163	Y-M: 20[redacted] / 65
VSL#3	1 CAPSULE	BID	Y-M: 20[redacted] / -155	ONGOING
FERROUS GLUCONATE	225 mg (milligram(s))	QD	Y-M: 20[redacted] / -7	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 65
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 37
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 47
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 54
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 55
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 65
ADALIMUMAB	40 mg (milligram(s))	OTHER: QOW	Y-M: 20[redacted] / 65	ONGOING
MORPHINE	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 65
SODIUM CHLORIDE	1000 mg (milligram(s))	OTHER: ONCE	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 65
KETOROLAC TROMETHAMINE	30 mg (milligram(s))	PRN	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
METHYLPREDNISOLONE SODIUM SUCCINATE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 67

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
OSMOTAN	250 ML/HOUR	OTHER: CONTINUOUS	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 67
PANTOPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 67
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 67	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 68	ONGOING

Event #1: Serious Adverse Event

Event Description	PANCREATITIS
Preferred term	膵炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 65 (22 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 65): ABS BASOS: 0.13 [0 - 0.1] K/UL; ABS EOS: 0.35 [0 - 0.3] K/UL; ABS IMMATURE GRANS: 0.16 [0 - 0.05] K/UL; ABS MONOS: 3.26 [0 - 1] K/UL; ABS NEUTS: 12.26 [1.5 - 8] K/UL; IMMATURE GRANS: 0.8 [0 - 0.6] %; LIPASE: 2201 [8 - 78] IU/L; MCHC: 31.5 [32 - 37] G/DL; SED RATE: 31 [0 - 15] MM/HR; [redacted]20[redacted] (RX DAY 66): ABS EOS: 0.46 [0 - 0.3] K/UL; ABS IMMATURE GRANS: 0.19 [0 - 0.05] K/UL; ABS MONOS: 3.03 [0 - 1] K/UL; ABS NEUTS: 11.07 [1.5 - 8] K/UL; IMMATURE GRANS: 1.1 [0 - 0.6] %; LIPASE: 830 [8 - 78] IU/L; [redacted]20[redacted] (RX DAY 67): LIPASE: 165 [8 - 78] IU/L; [redacted]20[redacted] (RX DAY 71): ABS NEUTS: 12.86 [1.5 - 8] K/UL; LIPASE: 254 [8 - 78] IU/L; [redacted]20[redacted] (RX DAY 79): ABS NEUTS: 14.09 [1.5 - 8] K/UL; LIPASE: 69 [8 - 78] IU/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 65): COMPLETE ABDOMINAL ULTRASOUND: NONVISUALIZATION OF THE PANCREAS SECONDARY TO OVERLYING BOWEL GAS, MILD SPLENOMEGALY MEASURING 13.2 CM, THE EXAMINATION IS OTHERWISE UNREMARKABLE.; [redacted]20[redacted] (RX DAY 66): MRI ABDOMEN WITHOUT CONTRAST/MRCP: MR FINDINGS COMPATIBLE WITH RELATIVELY MILD ACUTE PANCREATITIS, WITH QUESTIONABLE INCOMPLETE PANCREAS DIVISUM, FINDINGS CONSISTENT WITH GALLBLADDER SLUDGE, WITH OTHERWISE NO DISCRETE CHOLELITHIASISOR CHOLECYSTITIS.

AE Stopped Rx Day	79 (36 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男性（米国）であり，重篤な有害事象の膵炎を発現した。関連する病歴は，肥満，臍帯周囲の腹痛，鼓腸，間欠性の食欲喪失，間欠性の悪心，腹部膨満，胃炎，間欠性の嘔吐，潰瘍性大腸炎，潰瘍性大腸炎の再燃に伴う急性膵炎 2 回であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は非反応例であったため，治験薬の投与を中止した。
20[redacted] 年 [redacted] 月 [redacted] 日，膵炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，膵炎は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，急性の腹痛，複数回の非血性及び非胆汁性嘔吐，血性下痢並びに経口摂取減少が認められた。同日，消化管安静，静脈内水分補給，腹部超音波検査及び磁気共鳴画像検査のため，被験者は入院した。検査で心窩部領域に圧痛及び水分の嘔吐がみられたが，発熱又は胸痛は認められなかった。臨床検査の結果，白血球数（19.2）及び C 反応性たん白（2.5）の増加，並びに赤血球沈降速度 31 が認められ，リパーゼは 20[redacted] 年 [redacted] 月 [redacted] 日に 22 であったが，報告当時には 2201 に増加した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for HUMIRA (Blinded)

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1) Pancreatitis (10033645) (Pancreatitis (10033645)) [v.20.1] [10033645]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of PANCREATITIS

- Investigator: NOT APPLICABLE.

- AbbVie: RISK FACTORS INCLUDE PRIOR HISTORY OF ACUTE PANCREATITIS SECONDARY TO ULCERATIVE COLITIS FLARE, AND PRE-EXISTING ULCERATIVE COLITIS ITSELF.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ABS IMMATURE GRANS:** 0.16 KU/L (normal 0.0 to 0.05)

[redacted] 20[redacted] **ABS IMMATURE GRANS:** 0.19 KU/L (normal 0.0 to 0.05)

[redacted] 20[redacted] **ABS MONOS:** 3.26 KU/L (normal 0.0 to 1.00)

[redacted] 20[redacted] **ABS MONOS:** 3.03 KU/L (normal 0.0 to 1.00)

[redacted] 20[redacted] **ABS NEUTS:** 12.26 KU/L (normal 1.50 to 8.00)

[redacted] 20[redacted] **ABS NEUTS:** 11.07 KU/L (normal 1.50 to 8.00)

[redacted] 20[redacted] **ABS NEUTS:** 12.86 K/UL (normal 1.50 to 8.00)

[redacted] 20[redacted] **ABS NEUTS:** 14.09 K/UL (normal 1.50 to 8.00)

[redacted] 20[redacted] **COMPLETE ABDOMINAL ULTRASOUND:** NONVISUALIZATION OF THE PANCREAS SECONDARY TO OVERLYING BOWEL GAS, MILD SPLENOMEGALY MEASURING 13.2 CM, THE EXAMINATION IS OTHERWISE UNREMARKABLE.

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 2.5 mg/dL (normal 0.0 to 1.0)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.6 mg/dL (normal 0.0 to 1.0)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.4 mg/dL (normal 0 to 1.0)

[redacted] **20[redacted] LIPASE:** 2201 IU/L (normal 8 to 78)

[redacted] **20[redacted] LIPASE:** 830 IU/L (normal 8 to 78)

[redacted] **20[redacted] LIPASE:** 165 IU/L (normal 8 to 78)

[redacted] **20[redacted] LIPASE:** 254 IU/L (normal 8 to 78)

[redacted] **20[redacted] LIPASE:** 69 IU/L (normal 8 to 78)

[redacted] **20[redacted] MRI ABDOMEN WITHOUT CONTRAST/MRCP:** MR FINDINGS COMPATIBLE WITH RELATIVELY MILD ACUTE PANCREATITIS, WITH QUESTIONABLE INCOMPLETE PANCREAS DIVISUM, FINDINGS CONSISTENT WITH GALLBLADDER SLUDGE, WITH OTHERWISE NO DISCRETE CHOLELITHIASIS OR CHOLECYSTITIS.

[redacted] **20[redacted] PLATELET COUNT:** 542 K/UL (normal 150 to 450)

[redacted] **20[redacted] PLATELET COUNT:** 433 K/IL (normal 150 to 450)

[redacted] **20[redacted] SED RATE:** 31 MM/HR (normal 0 to 15)

[redacted] **20[redacted] WBC:** 19.23 KU/L (normal 4.5 to 12)

[redacted] **20[redacted] WBC:** 17.75 KU/L (normal 4.5 to 12)

[redacted] **20[redacted] WBC:** 16.73 K/UL (normal 4.50 to 12.00)

[redacted] **20[redacted] WBC:** 17.03 K/UL (normal 4.50 to 12.00)

Subject [redacted](Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHDOL	1[redacted]	FEMALE	MULTIPLE

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: SELF HARM	20[redacted]
UVEITIS: EXTRAINTESTINAL MANIFESTATION OF ACTIVE UC	20[redacted]
OTHER: PERSISTENT COUGH ATTRIBUTED TO SEASONAL ALLERGIES	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHDOL	[redacted]20[redacted] / 1	[redacted]20[redacted] / 29	42

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	3.6 g (gram(s))	QD	Y-M: 20[redacted] / -198
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -198
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -119
ERGOCALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted] / -118
DEXAMETHASONE	0.1 % (percent)	QID	Y-M: 20[redacted] / -25
PARACETAMOL	1 TABLET	OTHER: SINGLE USE	Y-M: 20[redacted] / -3

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	3.6 g (gram(s))	QD	Y-M: 20[redacted] / -198	Y-M: 20[redacted] / 56
ERGOCALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted] / -118	ONGOING
FLUCONAZOLE	150 mg (milligram(s))	OTHER: SINGLE USE	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 24
PARACETAMOL	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 37
DIMENHYDRINATE	50 mg (milligram(s))	OTHER: ONCE	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 41
CALCIUM CARBONATE	750 mg (milligram(s))	QD	Y-M: 20[redacted] / 42	ONGOING
PARACETAMOL	625 mg (milligram(s))	PRN	Y-M: 20[redacted] / 42	ONGOING
SODIUM CHLORIDE	1000 mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 51
METHYLPREDNISOLONE	15 mg (milligram(s))	OTHER: Q8 HOURS	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 51
ONDANSETRON	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 51
FERROUS GLUCONATE	300 mg (milligram(s))	BID	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 51
LANSOPRAZOLE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 51

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MACROGOL 3350	17 g (gram(s))	PRN	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 56
SODIUM CHLORIDE	1 SPRAY	QID	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 51
FLEET	133 mL (millilitre(s))	PRN	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 56
SENNA ALEXANDRINA	8.6 mg (milligram(s))	PRN	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 56
MORPHINE	5 mg (milligram(s))	PRN	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 55
IBUPROFEN	221 mg (milligram(s))	PRN	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 56
METRONIDAZOLE	500 mg (milligram(s))	OTHER: Q8 HOURS	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 56
HYDROCORTISONE	33 mg (milligram(s))	OTHER: Q8 HOURS	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
CEFTRIAXONE	2000 mg (milligram(s))	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 62
DIMENHYDRINATE	25 mg (milligram(s))	PRN	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 62
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 62
MORPHINE	3 mg (milligram(s))	PRN	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 58
KETOROLAC	15 mg (milligram(s))	PRN	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 59
FLEBOBAG RING LACT	500 mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 59
HYDROCORTISONE	33 mg (milligram(s))	TID	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 60
HYDROCORTISONE	17 mg (milligram(s))	TID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 62
HYDROCORTISONE	8 mg (milligram(s))	TID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 62
AMOXICILLIN W/CLAVULANATE POTASSIUM	1 TABLET	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 67

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

Event #1: Serious Adverse Event

Event Description	WORSENING UC SYMPTOMS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 36 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	

[redacted]20[redacted] (RX DAY 42): ABDOMINAL X-RAY: NO SMALL BOWEL OBSTRUCTION. INCREASED HAUSTRAL MARKINGS CONSISTENT WITH ACTIVE COLITIS.; [redacted]20[redacted] (RX DAY 56): SUBTOTAL COLECTOMY: PERFORMED WITHOUT ANY COMPLICATIONS. LAPAROSCOPIC SURGERY RESULTED IN ILEOSTOMY.

AE Stopped Rx Day	62 (33 DAYS AFTER LAST TREATMENT)
Duration of AE	27 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.

MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（カナダ）であり，重篤な有害事象の潰瘍性大腸炎症状の悪化が認められた。関連する病歴は，潰瘍性大腸炎及び活動性潰瘍性大腸炎の腸管外症状であった。被験者は非喫煙者であり，飲酒の習慣はなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎症状の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎症状の悪化は回復した。

有害事象発現前，被験者は潰瘍性大腸炎の突出症状のために入院したことがあった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，潰瘍性大腸炎症状の悪化と診断された。1 日 7～8 回の有痛性排便が認められ，このうちの 50%超が血性便であった。小児潰瘍性大腸炎活動性指標スコアは 80 であった。直近の 24 時間以内に嘔吐及びレッチングがみられ，間欠性の発熱を伴っていた。腹部の広範囲に軽度の筋性防御を伴う圧痛が認められ，腹壁反跳はみられなかった。軽度の頻脈も認められた。ステロイドが静脈内投与され，モニタリングされた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は

試験を中止した。20[redacted] 年 [redacted] 月 [redacted] 日，結腸亜全摘除及び回腸瘻造設が実施され，合併症はみられなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，Mezavant（メサラジン）の服薬アドヒアランス継続を促された。

治療薬として Tylenol（アセトアミノフェン），オンダンセトロン，Pentasa（メサラジン），メチルプレドニゾロン，prednisone，ジメンヒドリナート，モルヒネ，セフトリアキソン，イブプロフェン，ヒドロコルチゾン及びアモキシシリン／クラブラン酸が投与された。

The patient's past medications include:

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

TYLENOL for PERSISTENT COUGH ([redacted] 20[redacted] [redacted] 20[redacted])

FLUCONAZOLE for YEAST VAGINITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING UC SYMPTOMS

- Investigator: Not applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL X-RAY: No small bowel obstruction. Increased haustral markings consistent with active colitis.

[redacted] 20[redacted] C. DIFFICILE TEST: Negative

[redacted] 20[redacted] HEMOGLOBIN: 92 G/L (normal 120 to 150)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 10.8 MG/L (normal 0 to 5)

[redacted] 20[redacted] PEDIATRIC ULCERATIVE COLITIS ACTIVITY INDEX (PUCAI) SCORE: 80 No units

[redacted] 20[redacted] PLATELET COUNT: 619 X10**9/L (normal 150 to 400)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD-MSD	1[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: SIDEROPENIC ANEMIA	NOT REPORTED
OTHER: ASTHENIC HABITUS	NOT REPORTED
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MSD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 128	85

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -365
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -189
COLECALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted] / -153
METHYLPREDNISOLONE SODIUM SUCCINATE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -45
METHYLPREDNISOLONE SODIUM SUCCINATE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -43
OMEPRAZOLE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -41
POTASSIUM CHLORIDE	600 mg (milligram(s))	QD	Y-M: 20[redacted] / -41
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -41
SACCHARATED IRON OXIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -37
METHYLPREDNISOLONE SODIUM SUCCINATE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -30
FERRIC CARBOXYMALTOSE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -28
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -28
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -28
PICO-SALAX	1 DF (dosage form)	BID	Y-M: 20[redacted] / -22
DIAZEPAM	8 mg (milligram(s))	QD	Y-M: 20[redacted] / -21
PROPOFOL	1 DF (dosage form)	QD	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
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -365	-ONGOING
COLECALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted] / -153	-ONGOING
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -28	-ONGOING
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 51	-Y-M: 20[redacted] / 57
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 58	-Y-M: 20[redacted] / 64

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
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 65	Y-M: 20[redacted]-[redacted] / 71
PREDNISONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 72	Y-M: 20[redacted]-[redacted] / 78
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 78	Y-M: 20[redacted]-[redacted] / 85
METAMIZOLE SODIUM	500 mg (milligram(s))	OTHER: IN CASE OF FEVER	Y-M: 20[redacted]-[redacted] / 85	Y-M: 20[redacted]-[redacted] / 85
BLOOD AND RELATED PRODUCTS	243 mL (millilitre(s))	OTHER: PATIENT HAD BLOOD TRANSFUSION [redacted]/[redacted]/20[redacted] ONCE PER DAY	Y-M: 20[redacted]-[redacted] / 85	Y-M: 20[redacted]-[redacted] / 87
CIPROFLOXACIN	400 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 85	Y-M: 20[redacted]-[redacted] / 94
METRONIDAZOLE	350 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 85	Y-M: 20[redacted]-[redacted] / 94
PREDNISONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 86	Y-M: 20[redacted]-[redacted] / 92
FERRIC CARBOXYMALTOSE	500 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 91	Y-M: 20[redacted]-[redacted] / 91
CIPROFLOXACIN HYDROCHLORIDE	500 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 95	Y-M: 20[redacted]-[redacted] / 102
METRONIDAZOLE	250 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 95	Y-M: 20[redacted]-[redacted] / 108
SODIUM CHLORIDE	500 mL (millilitre(s))	OTHER: ACCORDING TO FLUID BALANCE	Y-M: 20[redacted]-[redacted] / 112	Y-M: 20[redacted]-[redacted] / 113
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 113	Y-M: 20[redacted]-[redacted] / 113
ELECTROLYTES NOS W/GLUCOSE	500 mL (millilitre(s))	OTHER: ACCORDING TO BALANCE OF FLUID AND IONS LEVEL	Y-M: 20[redacted]-[redacted] / 113	Y-M: 20[redacted]-[redacted] / 115
BLOOD AND RELATED PRODUCTS	1 TU	QD	Y-M: 20[redacted]-[redacted] / 128	Y-M: 20[redacted]-[redacted] / 129
AMINO ACIDS NOS W/ELECTROLYTES NOS/	1000 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 129	Y-M: 20[redacted]-[redacted] / 135
FERRIC CARBOXYMALTOSE	500 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 132	Y-M: 20[redacted]-[redacted] / 132
METHYLPREDNISOLONE SODIUM SUCCINATE	500 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 133	Y-M: 20[redacted]-[redacted] / 135

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
POTASSIUM CHLORIDE	600 mg (milligram(s))	QD	Y-M: 20[redacted] / 134	-ONGOING
PREDNISONE	60 mg (milligram(s))	QD	Y-M: 20[redacted] / 136	-ONGOING
ALPRAZOLAM	0.25 mg (milligram(s))	OTHER: 1/2-1/2-1	Y-M: 20[redacted] / 139	-ONGOING

Event #1: Serious Adverse Event

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 85
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	87
Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	IS DUE TO ACUTE ENTERITIS, CONCICTENCY OF STOOL WORSENED AND NOW STOOL IS WITH BLOOD ALSO
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

Event #2: Serious Adverse Event

Event Description	ACUTE ENTERITIS
Preferred term	小腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 85
Age at AE Onset	1[redacted]
Laboratory Testing	
[redacted]20[redacted](RX DAY 85): C-REACTIVE PROTEIN: 18.5 [0 - 10] MG/L; IRON: 2.6 [11 - 28] MCMOL/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	97
Duration of AE	13 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COULD BE RANDOM VIRAL INFECTION CAUSE ACUTE ENTERITIS; COULD BE REACTIVATION OF CMV COLITIS BECAUSE PATIENT IS UNDER IMMUNOSUPPRESSIVE DRUGS;
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #3: Serious Adverse Event

Event Description	ACUTE GASTROENTERITIS
Preferred term	胃腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 112
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	120
Duration of AE	9 DAYS
Severity	MODERATE

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ACUTE GASTROENTERITIS DUE TO VIRAL OR BACTERIAL INFECTION OR RELAPS OF UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Event Description	SEVERE ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 128
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	147 (19 DAYS AFTER LAST TREATMENT)
Duration of AE	20 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FLARE OF UC
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, LIFE THREATENING

Event #5: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 128
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	147 (19 DAYS AFTER LAST TREATMENT)
Duration of AE	20 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CAN BE IN RELATIONSHIP TO ABSENCE OF STUDY DRUG
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).

FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男性（スロバキア共和国）であり，重篤な有害事象の急性小腸炎及び貧血を発現した。関連する病歴は，潰瘍性大腸炎及び鉄欠乏性貧血であった。
20[redacted] 年 [redacted] 月 [redacted] 日，急性小腸炎及び貧血が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，下痢が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 1 回嘔吐し，同日に入院した。被験者は疲労感，体重減少，肌の青白さ，水性下痢及び発熱を訴えた。入院中，輸血及び抗生剤の投与が行われた。治療後に体調は大幅に改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。同日に急性小腸炎は回復した。
治療薬としてメトロニダゾール，シプロフロキサシン，Novalgin，Ciprolon（シプロフロキサシン塩酸塩水和物），Entizol（メトロニダゾール），Ferinject（カルボキシマルトース第二鉄）及びオメプラゾールが投与された。
また，生理食塩水及びイオンを含む 5%ブドウ糖液も投与された。

The patient's past medications include:

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

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

HELICID for USING CORTICOIDS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

FERINJECT for IMPROVEMENT OF BLOOD COUNT ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Enteritis (10014866) (Enteritis (10014866)) [v.20.1] [10014866]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Anemia (10002272) (Anaemia (10002034)) [v.20.1] [10002272]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ACUTE ENTERITIS

- Investigator: Could be random vial infection cause acute enteritis. Could be reactivation of CMV colitis because patient is under immunosuppressive drugs.

- AbbVie: Exacrebation of underlyiong disease VS acute gastroenteritis

Event of ANEMIA

- Investigator: Is due to acute enteritis, consistency of stool worsened and now stool is with blood also

- AbbVie: Complication from Underlying disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] C REACTIVE PROTEIN: 18.5 mg/l (normal 0.00 to 10.0)

[redacted] 20[redacted] CALCIUM: 2.18 mmol/l (normal 2.25 to 2.85)

[redacted] 20[redacted] HEMOGLOBIN: 6.3 G/DL (normal 13.5 to 17.5)

[redacted] 20[redacted] IRON: 2.6 mcmol/l (normal 11.0 to 28.0)

[redacted] 20[redacted] PLATELET COUNT: 580 X10**9/L (normal 150 to 400)

[redacted] 20[redacted] RBC: 3.2 x 10^12/L (normal 4.0 to 5.0)

[redacted] 20[redacted] WBC: 15.49 X10**9/L (normal 4.0 to 10.0)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男性（スロバキア共和国）であり，重篤な有害事象の急性胃腸炎を発現した。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，急性胃腸炎が発現した。同日，被験者は発熱を伴う胃腸炎のため入院した。急性胃腸炎，発熱，イオン不均衡及び炎症マーカー低値を含む徴候及び症状が認められ，生理食塩水及びイオンを含む 5%ブドウ糖液を静脈内投与したところ，臨床状態は改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
20[redacted] 年 [redacted] 月 [redacted] 日，急性胃腸炎は回復した。
治療薬としてオメプラゾール，生理食塩水及びイオンを含む 5%ブドウ糖液が投与された。

The patient's past medications include:

HELICID for BECAUSE HE IS USING CORTICOIDS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for HUMIRA (Blinded)

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1) Acute gastroenteritis (10066762) (Gastroenteritis (10017888)) [v.18.1] [10066762]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ACUTE GASTROENTERITIS

- Investigator: Acute gastroenteritis due to viral or bacterial infection or relapse of UC.

- AbbVie: Ecacerbation of underlying UC

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男性（スロバキア共和国）であり，重篤な有害事象の高度の貧血及び潰瘍性大腸炎の再燃が認められた。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎及び鉄欠乏性貧血であった。

20[redacted] 年 [redacted] 月 [redacted] 日，高度の貧血及び潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，高度の貧血及び潰瘍性大腸炎の再燃は回復した。

投与 18 週時の規定来院中，肌の青白さ，疲労感及び両足首浮腫がみられた。ヘモグロビン低値及び大量の血液を伴う水様便も認められた。ヘモグロビンは 54 g/L，血清アルブミンは 2.1 g/dL であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，高度の貧血及び潰瘍性大腸炎の再燃により，輸血を受けるため入院した。同日，アダリムマブの投与は中止された。コルチコステロイドによる代替療法が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療として輸血，並びに Periolimel，Solu-medrol（メチルプレドニゾロンコハク酸エステルナトリウム），prednisone 及び Ferinject（カルボキシマルトース第二鉄）の投与が行われた。

The patient's past medications include:

SALOFALK for ULCERATIVE COLITIS ([redacted])

PREDNISON for ULCERATIVE COLITIS ([redacted])

VENOFER for ULCERATIVE COLITIS ([redacted])

BLOOD TRANSFUSION for ANEMIA ([redacted])

NOVALGIN for FEVER ([redacted])

ENTIZOL for ACUTE ENTERITIS ([redacted])

Causality for HUMIRA (Blinded)

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1) Anemia (10002272) (Anaemia (10002034)) [v.18.1] [10002272]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

2) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.18.1] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of SEVERE ANEMIA

- Investigator: Flare of ulcerative colitis.

- AbbVie: History of anemia and exacerbation of ulcerative colitis.

Event of UC FLARE

- Investigator: Can be in relationship to absence of study drug

- AbbVie: A flare of the underlying ulcerative colitis.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
胃腸炎	X			
小腸炎		X		

Treatment Group	Age at Study Start	Sex	Race
ISD-MSD	1[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: ACNE VULGARIS, FACE, BACK, SHOULDERS	NOT REPORTED
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	55
MSD	[redacted]20[redacted] / 56	[redacted]20[redacted] / 119	77

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CALCIUM CARBONATE	600 mg (milligram(s))	QD	Y-M: 20[redacted] / -192
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -192
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -93
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -93
CIPROFLOXACIN	400 mg (milligram(s))	BID	Y-M: 20[redacted] / -81
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / -81
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -75
OMEPRAZOLE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -72
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / -71
OMEPRAZOLE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -71
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -55
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -48
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -41
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -34
PICO-SALAX	1 DF (dosage form)	BID	Y-M: 20[redacted] / -23
DIAZEPAM	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -22
PROPOFOL	1 DF (dosage form)	QD	Y-M: 20[redacted] / -22
SEVOFLURANE	1 DF (dosage form)	QD	Y-M: 20[redacted] / -22
ESCHERICHIA COLI	100 mg (milligram(s))	QD	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
CALCIUM CARBONATE	600 mg (milligram(s))	QD	Y-M: 20[redacted] / -192	ONGOING
ESCHERICHIA COLI	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -21	ONGOING
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 42
PREDNISONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 49
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 56
PREDNISONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 63
RIFAXIMIN	200 mg (milligram(s))	TID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 79
CIPROFLOXACIN HYDROCHLORIDE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 99
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 99

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
XYLOMETAZOLINE HYDROCHLORIDE	1 gtt (drop(s))	QD	Y-M: 20[redacted] / 103	Y-M: 20[redacted] / 103
IBUPROFEN	200 mg (milligram(s))	QD	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 106

Event #1: Serious Adverse Event

Event Description	ACUTE GASTROENTERITIS
Preferred term	胃腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 68
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	72
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ACQUIRED VIRAL OR BACTERIAL INFECTION, REACTIVATION OF UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	ENTERITIS
Preferred term	小腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 83
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	

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

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every

week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男児（スロバキア共和国）であり，重篤な有害事象の急性胃腸炎を発現した。関連する病歴は，潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，急性胃腸炎が発現した。同日，水様便の頻度増加及び軟度の悪化がみられ，被験者は入院した。Normix（リファキシミン）を投与したところ，軽快がみられた。便培養の結果は陰性であり，ウイルス感染は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。同日，急性胃腸炎は回復した。
治療薬として Entizol（メトロニダゾール），Normix（リファキシミン）及び Ciphin（シプロフロキサシン塩酸塩水和物）が投与された。

The patient's past medications include:

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

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

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

Causality for HUMIRA (Blinded)

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1) Acute gastroenteritis (10066762) (Gastroenteritis (10017888)) [v.18.1] [10066762]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ACUTE GASTROENTERITIS

- Investigator: Acquired viral or bacterial infection reactivation of UC.

- AbbVie: N/A

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD-MHD-FREIND	[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: ANAEMIA DUE TO ULCERATIVE COLITIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: SINCE 20[redacted]	20[redacted]
MURMUR: FUNCTIONAL MURMUR WITHOUT CHANGES IN ECHOCARDIOGRAPHY	20[redacted]
OTHER: UNDERWEIGHT	20[redacted]
TRANSFUSIONS: PATIENT REQUIRED TRANSFUSION DUE TO ANAEMIA IN DECURSU ULCERATIVE COLITIS	20[redacted]
Ulcerative colitis	20[redacted]
PANCREATITIS: TWICE 1. IDIOPATHIC 2. DUE TO IMMUNOSUPPRESSANT USE	20[redacted]
OTHER: GROWTH FAILURE	20[redacted]
SKIN DISORDERS: HIRSUTISM	20[redacted]
HYPERTENSION: DIAGNOSED AND TREATED DUE TO HYPERTENSION	20[redacted]
MIGRAINE HEADACHE: HEADACHE PROPABLY DUE TO HYPERTENSION	20[redacted]
SURGERY: WOUND OF LEFT UPPER LEG(SUTURED)	20[redacted]
OTHER: NYCTURIA	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted] / 1	[redacted] / 43	56
MHD	[redacted] / 57	[redacted] / 78	28
FREIND	[redacted] / 85	[redacted] / 197	117
2nd FLARE OL ADA	[redacted] / 202	[redacted] / 358	170

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CROMOGLICATE SODIUM	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
COLECALCIFEROL	500 IU (international unit(s))	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BISOPROLOL FUMARATE	1,25 mg (milligram(s))	QD	Y-M: 20[redacted] / -199
METHYLPREDNISOLONE	8 mg (milligram(s))	QD	Y-M: 20[redacted] / -148
POTASSIUM	10 mL (millilitre(s))	BID	Y-M: 20[redacted] / -118
VANCOMYCIN	250 mg (milligram(s))	QID	Y-M: 20[redacted] / -36
CIPROFLOXACIN	250 mg (milligram(s))	BID	Y-M: 20[redacted] / -20
SMECTA	1 SACH.	BID	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
COLECALCIFEROL	500 IU (international unit(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 526
BISOPROLOL FUMARATE	1,25 mg (milligram(s))	QD	Y-M: 20[redacted] / -199	ONGOING
POTASSIUM	10 mL (millilitre(s))	BID	Y-M: 20[redacted] / -118	ONGOING
METHYLPREDNISOLONE	2 mg (milligram(s))	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 69
SMECTA	1 SACH	BID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 73
METHYLPREDNISOLONE	6 mg (milligram(s))	QD	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 73

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
SMECTA	1 SACH	TID	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 91
METHYLPREDNISOLONE	8 mg (milligram(s))	QD	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 109
METHYLPREDNISOLONE	6 mg (milligram(s))	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 114

Event #1: Serious Adverse Event

Event Description	FLARE OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 85
Age at AE Onset	[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY -6): NITR: NEG [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 85): AMYLASA: 54 [25 - 125] U/L; CRP: 11.8 [0.2 - 5] MG/L; D-DIMERS: 0.37 [0 - 0.5] UG/ML; FIBRINOGEN: 4.08 [2 - 4.5] G/L; IRON: 2.8 [8.9 - 21.4] UMOL/L; LEU: 6 [0 - 15] /UL; LIPASE: 4 [0 - 78] U/L; MAGNESIUM: 2.15 [1.7 - 2.1] MG/DL; SR: 25 [3 - 8] MM/HR

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	110
Duration of AE	26 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ULCERATIVE COLITIS EXACERBATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and

Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted]20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，[redacted] 歳の男児（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，小児潰瘍性大腸炎（左側）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。潰瘍性大腸炎の増悪，半液状便の増加（最高 9 回）及び血便がみられた。被験者は高度の疾患，早期発症及びステロイド依存のリスク因子を有していた。治験薬の投与を再開後に軽快が認められた。

The patient's past medications include:

NATRII CROMOGLICAS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

VANCOMYCIN for ULCERATIVE COLITIS EXACERBATION ([redacted] 20[redacted] - [redacted] 20[redacted])

CIPROFLOXACIN for ULCERATIVE COLITIS EXACERBATION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of FLARE OF ULCERATIVE COLITIS

- Investigator: ulcerative colitis exacerbation.- AbbVie: The underlying UC

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BASOPHILS: 0.3 % (normal 0 to 1)

[redacted] 20[redacted] CREATININE: 0.37 mg/dL (normal 0.73 to 1.18)

[redacted] 20[redacted] CRP: 11.8 MG/L (normal 0.2 to 5)

[redacted] 20[redacted] Electrocardiogram: Abnormal: Rhythm

[redacted] 20[redacted] EOSINOPHILS: 0.1 % (normal 1 to 5)

[redacted] 20[redacted] FIBRINOGEN: 4.08 G/L (normal 2 to 4.5)

[redacted] 20[redacted] GLUCOSE: 77 mg/dL (normal 70 to 99)

[redacted] 20[redacted] GLUCOSE (URINALYSIS): Negative

[redacted] 20[redacted] HEMATOCRIT: 37.5 % (normal 35 to 45)

[redacted] 20[redacted] IRON: 2.8 umol/l (normal 8.9 to 21.4)

[redacted] 20[redacted] LYMPHOCYTES: 10.6 % (normal 25 to 50)

[redacted] 20[redacted] MONOCYTES: 3.5 % (normal 1 to 11)

[redacted] 20[redacted] NEUTROPHILS: 85.5 % (normal 25 to 60)

[redacted] 20[redacted] PLATELET COUNT: 530 X10**3/MCL (normal 130 to 400)

[redacted] 20[redacted] POTASSIUM: 4.3 MMOL/L (normal 3.8 to 5)

[redacted] 20[redacted] SGOT/AST: 13 U/L (normal 0 to 45)

[redacted] 20[redacted] SGPT/ALT: 10 U/L (normal 0 to 40)

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

[redacted] 20[redacted] SR: 25 MM/HR (normal 3 to 8)

[redacted] 20[redacted] URINE BLOOD: Negative

[redacted] 20[redacted] URINE KETONES: Negative

[redacted] 20[redacted] URINE LEU: 6 uL (normal 0 to 15)

[redacted] 20[redacted] URINE NITR: Negative

[redacted] 20[redacted] URINE PH: 7.5 No units (normal 4.5 to 7.5)

[redacted] 20[redacted] URINE SPECIFIC GRAVITY: 1002 No units (normal 1015 to 1025)

[redacted] 20[redacted] WBC: 15.29 X10**3/MCL (normal 4.5 to 13.5)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD-MPL	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
ASTHMA/REACTIVE AIRWAY DISEASE: BRONCHIAL ASTHMA	20[redacted]
PEPTIC ULCER DISEASE: CHRONIC GASTRITIS. HELICOBACTER PYLORI INFECTION	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
INFLAMMATORY BOWEL DISEASE: ANAL FISSURA	20[redacted]
ANEMIA: SIDEROPENIC ANAEMIA	20[redacted]
MURMUR: HEART MURMUR	20[redacted]
SYNCOPE: EPISODES OF SYNCOPE	20[redacted]
MIGRAINE HEADACHE: HEADACHE, TICKS	20[redacted]
OTHER: LEFT-SIDE CYST OF ETHMOID SINUS	20[redacted]
OTHER: WEIGHT AND HEIGHT DEFICIENCY	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: DENTAL CARIES	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted] / 1	[redacted] / 43	56
MPL	[redacted] / 57	[redacted] / 358	310

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	1000 mg (milligram(s))	BID	Y-M: [redacted]
COLECALCIFEROL	1000 mg (milligram(s))	QD	Y-M: [redacted]
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: [redacted] / -51
POTASSIUM CHLORIDE	391 mg (milligram(s))	QD	Y-M: [redacted] / -51
PREDNISONE	20 mg (milligram(s))	QD	Y-M: [redacted] / -51
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: [redacted] / -48

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / / RX Day	Stop Year-Month / RX Day
SULFASALAZINE	1000 mg (milligram(s))	BID	Y-M: [redacted]	ONGOING
COLECALCIFEROL	1000 mg (milligram(s))	QD	Y-M: [redacted]	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: [redacted] / - 48	ONGOING
TRIAMCINOLONE ACETONIDE	1 DF (dosage form)	BID	Y-M: [redacted] / 129	Y-M: [redacted] / 147
BETADERMIC	DOSE - OINTMENT DOSE - OINTMENT	BID	Y-M: [redacted] / 140	Y-M: [redacted] / 147
DITHRANOL	DOSE - OINTMENT OINTMENT - DOSE	BID	Y-M: [redacted] / 140	Y-M: [redacted] / 147
LORINDEN A	DOSE - OINTMENT DOSE - OINTMENT	BID	Y-M: [redacted] / 140	Y-M: [redacted] / 147
PARACETAMOL	500 mg (milligram(s))	QD	Y-M: [redacted] / 144	Y-M: [redacted] / 145

Event #1: Serious Adverse Event

Event Description	PSORIASIS
Preferred term	乾癬
AE Onset Date / Rx Day	[redacted] / 128
Age at AE Onset	[redacted]
Laboratory Testing	

NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	147
Duration of AE	20 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).

FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の乾癬を発現した。関連する病歴は，潰瘍性大腸炎であった。
本試験では，すべての被験者が最初の 8 週間にアダリムマブの投与を受け，投与 8 週時に維持療法期アダリムマブ高用量，維持療法期アダリムマブ標準用量又はプラセボのいずれかに無作為に割り付けられた。
20[redacted] 年 [redacted] 月 [redacted] 日，乾癬が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，乾癬は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，投与 18 週時の規定来院で乾癬と診断された。同日，被験者は救急で皮膚科医の診察を受けるため，待機的に入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は管理上の理由のため退院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は皮膚科クリニックに再入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Lorinden A，アセトアミノフェン，Diprosalic，Mediderm 及び Cygnoline ointment 1/16-1/8%が投与された。

The patient's past medications include:

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

Causality for HUMIRA (Blinded)

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1) Psoriasis (10037153) (Psoriasis (10037153)) [v.21.1] [10037153]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of PSORIASIS

- Investigator: Not applicable

- AbbVie: Not applicable

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
消化不良	X			

Treatment Group	Age at Study Start	Sex	Race
IHD-MHD	1[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANAEMIA	20[redacted]
OBESITY: OBESITY	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: STREPTOCOCCUS ALLERGISATION	20[redacted]
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	20[redacted]
OTHER: VITAMIN D3 DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]0[redacted] / 43	56
MHD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	308

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
COLECALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted]-[redacted] / -161
MESALAZINE	1500 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -161
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -45
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -27

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
COLECALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted]-[redacted] / 161	- ONGOING
MESALAZINE	1500 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 161	- ONGOING
ELECTROLYTE SOLUTIONS	500 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 364	Y-M: 20[redacted]-[redacted] / 364
GLUCOSE	20 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 364	Y-M: 20[redacted]-[redacted] / 364
RECTANAL	150 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 364	Y-M: 20[redacted]-[redacted] / 365
ELECTROLYTE SOLUTIONS	250 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 365	Y-M: 20[redacted]-[redacted] / 365

Event #1: Serious Adverse Event

Event Description	FUNCTIONAL DYSPEPSIA
Preferred term	消化不良
AE Onset Date / Rx Day	[redacted]20[redacted] / 364 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 365): GASTRODUODENOSCOPY: NORMAL PICTURE OF THE ESOPHAGUS, STOMACH AND DUODENUM

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FUNCTIONAL DYSPEPSIA PROBABLY AFTER DIETETICAL MISTAKE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second

disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted]20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の機能性ディスペプシアを発現した。関連する病歴は，肥満，潰瘍性大腸炎，レンサ球菌のアレルギー化及びクロストリジウム・ディフィシレ感染であった。被験者は非喫煙者及び非アルコール摂取者であった。
20[redacted] 年 [redacted] 月 [redacted] 日，機能性ディスペプシアが発現した。20[redacted] 年 [redacted] 月 [redacted] 日，機能性ディスペプシアは回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，おそらく「誤食（dietetical mistake）」に関連した上腹部痛のため入院した。上部消化管内視鏡検査が実施され，結果は正常であったが，機能性ディスペプシアの診断が下された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

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

METRONIDAZOL for EXACERBATION OF ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

METRONIDAZOL for EXACERBATION OF ULCERATIVE COLITIS

Causality for HUMIRA (Blinded)

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1) Functional dyspepsia (10064536) (Dyspepsia (10013946)) [v.22.0] [10064536]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of FUNCTIONAL DYSPEPSIA

- Investigator: Functional dyspepsia probably after dietetical mistake.

- AbbVie: Development of the event is not consistent with study drug's mechanism of action. Additionally the event appears to be related to dietary choices.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] GASTRODUODENOSCOPY: Normal picture of the esophagus, stomach and duodenum.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD-MHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
FEEDING DISORDERS/DIETARY INTOLERANCES: LACTOSE INTOLERANCE	20[redacted]
GASTROINTESTINAL BLEED: RECTAL BLEEDING	20[redacted]
OTHER: VITAMIN D3 DEFICIENCY	20[redacted]
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MHD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	308

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
COLECALCIFEROL	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -224
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -133
AZATHIOPRINE	37.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -45
METHYLPREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -42
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / -27

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
COLECALCIFEROL	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -224	ONGOING
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -133	ONGOING
AZATHIOPRINE	37.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -45	ONGOING
LEVOCETIRIZINE DIHYDROCHLORIDE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 287
AMBROXOL HYDROCHLORIDE	15 mg (milligram(s))	BID	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 292
ANDROGRAPHIS PANICULATA LEAF W/GENTIANA SPP.	1 DF (dosage form)	QD	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 292
SODIUM CHLORIDE	2 DF (dosage form)	BID	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 292
CIRRUS	5 mg (milligram(s))	BID	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 308
MOMETASONE FUROATE	50 mcg (microgram(s))	BID	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 308

Event #1: Serious Adverse Event

Event Description	FRACTURE OF THE PROXIMAL PHALANX OF THE 5TH FINGER OF THE LEFT PALMA WITH THE TRANSLOCATION
Preferred term	手骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 315
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 315): SURGERY - INTRODUCTION OF THE KIRSCHNER WIRE: [redacted]20[redacted] - SURGERY (REMOVAL OF THE KIRSCHNER WIRE

AE Stopped Rx Day	346
Duration of AE	32 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	TRAUMA WITH FOOTBALL BALL
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).

FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の変位を伴う左手掌第 5 指基節骨骨折を発現した。関連する病歴は，ビタミン D3 欠乏及び潰瘍性大腸炎（左側）であった。被験者は非喫煙者であり，飲酒の習慣はなかった。
20[redacted] 年[redacted] 月[redacted] 日，変位を伴う左手掌第 5 指基節骨骨折が発現した。20[redacted] 年[redacted] 月[redacted] 日，変位を伴う左手掌第 5 指基節骨骨折は回復した。
20[redacted] 年[redacted] 月[redacted] 日，被験者は入院し，骨折部位の固定のため，キルシュナー鋼線刺入術を受けた。20[redacted] 年[redacted] 月[redacted] 日，被験者は再入院した。20[redacted] 年[redacted] 月[redacted] 日，骨折部位の固定を解除し，キルシュナー鋼線を外科的に抜去した。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。

Causality for HUMIRA (Blinded)

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1) Fractured finger (10017286) (Hand fracture (10019114)) [v.21.0] [10017286]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for HUMIRA (Blinded)

Event of FRACTURE OF THE PROXIMAL PHALANX OF THE 5TH FINGER OF THE LEFT PALMA WITH THE TRANSLOCATION

- Investigator: TRAUMA WITH FOOTBALL BALL

- AbbVie: EVENT IS MORE LIKELY RELATED TO TRAUMATIC INJURY FROM FOOTBALL.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HEMATOCRIT: 32.2 % (normal 35.0 to 45.0)

[redacted] 20[redacted] HEMOGLOBIN: 10.1 G/DL (normal 12 to 15)

[redacted] 20[redacted] PLATELET COUNT: 297 X10**9/L (normal 140 to 420)

[redacted] 20[redacted] RBC (HEMATOLOGY): 4.30 T/l (normal 4.00 to 5.30)

[redacted] 20[redacted] WBC (HEMATOLOGY): 8.44 X10**9/L (normal 4.50 to 13.5)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD	1[redacted]	MALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 40	53

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -87
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -56
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / -56
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -56
COLECALCIFEROL	2 gtt (drop(s))	QD	Y-M: 20[redacted] / -14
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
POTASSIUM CHLORIDE	1 TABLET	QD	Y-M: 20[redacted] / -14
PREDNISONE	5 mg (milligram(s))	QD	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
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -87	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -56	ONGOING
COLECALCIFEROL	2 gtt (drop(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 33
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 33
POTASSIUM CHLORIDE	1 TABLET	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 33
PREDNISONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 33
INFLIXIMAB	250 mg (milligram(s))	OTHER: ACCORDING TO INFLIXIMAB THERAPY RULES	Y-M: 20[redacted] / 58	ONGOING

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 57 (17 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	

NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	81 (41 DAYS AFTER LAST TREATMENT)
Duration of AE	25 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second

disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男児（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められ，同日に被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
20[redacted] 年 [redacted] 月 [redacted] 日（投与 8 週時），被験者は試験を中止した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。
治療薬としてインフリキシマブが投与された。

The patient's past medications include:

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

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

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

KALIPOZ PROLONGATUM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

VITAMINUM D3 for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ULCERATIVE COLITIS FLARE

- Investigator: UC Flare

- AbbVie: The underlying UC

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -318
CICLOSPORIN	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -301
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -289

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / - 289	ONGOING
CIPROFLOXACIN HYDROCHLORIDE	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 56
ENOXAPARIN SODIUM	0.2 mL (millilitre(s))	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 56
SACCHAROMYCES BOULARDII	1 DF (dosage form)	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 56
GLUCOSE	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 48
CICLOSPORIN	150 mg (milligram(s))	QD	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
CICLOSPORIN	350 mg (milligram(s))	OTHER: 200 MG + 150 MG	Y-M: 20[redacted] / 50	ONGOING
GLUCOSE	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 51
RED BLOOD CELLS, CONCENTRATED	300 mL (millilitre(s))	QD	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
FERROUS SULFATE	1 DF (dosage form)	BID	Y-M: 20[redacted] / 56	ONGOING
FOLIC ACID	1 DF (dosage form)	QD	Y-M: 20[redacted] / 56	ONGOING
MAGNESIUM ASPARTATE	1 DF (dosage form)	QD	Y-M: 20[redacted] / 56	ONGOING
VITAMINUM	1 DF (dosage form)	QD	Y-M: 20[redacted] / 56	ONGOING

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

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 47 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	56 (14 DAYS AFTER LAST TREATMENT)
Duration of AE	10 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC FLARE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).

FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，高度の広範囲の潰瘍性大腸炎／汎大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，胃痛及び血便の徴候及び症状が認められたため，被験者は入院した。本事象は，アダリムマブによる生物学的療法の有効性欠如のため発現したものであり，治療薬としてシクロスポリンが投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
関連するリスク因子には原疾患があった。
治療薬としてシプロフロキサシン，Clexan（エノキサパリンナトリウム），ビタミン B 製剤，Enterol，濃厚赤血球，5%ブドウ糖，Asmag，Sorbifer durules（アスコルビン酸／硫酸鉄水和物），Acidum folicum（葉酸）及びシクロスポリンが投与された。

The patient's past medications include:

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

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

Causality for HUMIRA (Open Label)

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1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.19.0] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of UC FLARE

- Investigator: Ulcerative colitis flare.

- AbbVie: The underlying UC.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
SULFASALAZINE	2 TABLETS	QID	Y-M: 20[redacted] / -253
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -243
COLECALCIFEROL	2000 JM	QD	Y-M: 20[redacted] / -14
PICO-SALAX	150 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
FENTANYL	0.075 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
PARACETAMOL	1 g (gram(s))	QD	Y-M: 20[redacted] / -13
PROPOFOL	200 mg (milligram(s))	QD	Y-M: 20[redacted] / -13

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SULFASALAZINE	2 TABLETS	QID	Y-M: 20[redacted] / -253	ONGOING
COLECALCIFEROL	2000 JM	QD	Y-M: 20[redacted] / -14	ONGOING
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -13	ONGOING
FERRIC PYROPHOSPHATE	20 mg (milligram(s))	TID	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
OMEPRAZOLE	1 TABLET	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
POTASSIUM CHLORIDE	1 TABLET	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
BLOOD AND RELATED PRODUCTS	2 DF (dosage form)	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 35

Event #1: Serious Adverse Event

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 29
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	

NOT REPORTED	
AE Stopped Rx Day	36
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNDERLYING DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every

week.

3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.

Generated: [redacted]20[redacted]:01:48

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の貧血を発現した。関連する病歴は，左側潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，貧血が発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，ヘモグロビン低値のため輸血が行われ，同日に被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。

治療薬として Actiferol（ピロリン酸第二鉄）が投与された。

The patient's past medications include:

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

ENCORTON for ULCERATIVE COLITIS (Started [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Anemia (10002272) (Anaemia (10002034)) [v.20.1] [10002272]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ANEMIA

- Investigator: UNDERLYING DISEASE

- AbbVie: A COMMON COMPLICATION OF THE UNDERLYING UC

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Rectum/Sigmoid = 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions), Presence of friability - yes

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
頭痛	X			
意識消失	X			

Treatment Group	Age at Study Start	Sex	Race
ISD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
COGNITIVE, BEHAVIORAL OR PSYCHIATRIC DISORDER: BRIEF LOSS OF CONTACT AND ABNORMAL EEG AROUND AGE 5. TX WITH VALPROIC ACID.	20[redacted]
COGNITIVE, BEHAVIORAL OR PSYCHIATRIC DISORDER: ELECTIVE MUTISM	20[redacted]
COGNITIVE, BEHAVIORAL OR PSYCHIATRIC DISORDER: OBSERVATION FOR ANXIETY/ADJUSTMENT DISORDE	20[redacted]
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted] / 1	[redacted] / 42	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1.5 g (gram(s))	BID	Y-M: [redacted]
CITALOPRAM HYDROBROMIDE	20 mg (milligram(s))	QD	Y-M: [redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: [redacted] / -45
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: [redacted] / -44

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1.5 g (gram(s))	BID	Y-M: [redacted]	ONGOING
CITALOPRAM HYDROBROMIDE	20 mg (milligram(s))	QD	Y-M: [redacted]	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: [redacted] / -44	ONGOING
CHLORPROTHIXENE	7.5 mg (milligram(s))	QD	Y-M: [redacted] / 52	ONGOING
ACICLOVIR SODIUM	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
BENZYLPENICILLIN	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
BENZYLPENICILLIN SODIUM	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
CEFOTAXIME SODIUM	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
DEXAMETHASONE SODIUM PHOSPHATE	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
DIAZEPAM	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
KETOPROFEN	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
MANNITOL	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
MIDAZOLAM HYDROCHLORIDE	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68
NALBUPHINE HYDROCHLORIDE	UNK UNK	OTHER: UNK	Y-M: [redacted] / 52	Y-M: [redacted] / 68

			52
OMEPRAZOLE	UNK UNK	OTHER: UNK	Y-M: 20[redacted]- / Y-M: 20[redacted]- / 68 52
ONDANSETRON	UNK UNK	OTHER: UNK	Y-M: 20[redacted]- / Y-M: 20[redacted]- / 68 52
PARACETAMOL	UNK UNK	OTHER: UNK	Y-M: 20[redacted]- / Y-M: 20[redacted]- / 68 52

Event #1: Serious Adverse Event

Event Description	HEADACHES, LOSS OF CONSCIOUSNESS
Preferred term	頭痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 52 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 52): MAGNESIUM: 19.4 [NOT REPORTED - NOT REPORTED] MG/L; [redacted]20[redacted] (RX DAY 53): HS TROPONINE I: <5 [NOT REPORTED - NOT REPORTED] NG/L

Microbiology

[redacted]20[redacted] (RX DAY 21): Blood CEREBRAL FLUID CULTURE: -NOT DONE; [redacted]20[redacted] (RX DAY 52): Blood BLOOD CULTURE: -NOT DONE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 52): CHEST RAY: NORMAL; CT CNS: NORMAL; [redacted]20[redacted] (RX DAY 54): MR CNS: NORMAL; [redacted]20[redacted] (RX DAY 57): EEG: NORMAL; [redacted]20[redacted] (RX DAY 68): ECG HOLTER: NORMAL; ECHO: NORMAL

AE Stopped Rx Day	68 (26 DAYS AFTER LAST TREATMENT)
Duration of AE	17 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	HEADACHES, LOSS OF CONSCIOUSNESS
Preferred term	意識消失
AE Onset Date / Rx Day	[redacted]20[redacted] / 52 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 52): MAGNESIUM: 19.4 [NOT REPORTED - NOT REPORTED] MG/L; [redacted]20[redacted] (RX DAY 53): HS TROPONINE I: <5 [NOT REPORTED - NOT REPORTED] NG/L

Microbiology

[redacted]20[redacted] (RX DAY 21): Blood CEREBRAL FLUID CULTURE: -NOT DONE; [redacted]20[redacted] (RX DAY 52): Blood BLOOD CULTURE: -NOT DONE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 52): CHEST RAY: NORMAL; CT CNS: NORMAL; [redacted]20[redacted] (RX DAY 54): MR CNS: NORMAL; [redacted]20[redacted] (RX DAY 57): EEG: NORMAL; [redacted]20[redacted] (RX DAY 68): ECG HOLTER: NORMAL; ECHO: NORMAL

AE Stopped Rx Day	68 (26 DAYS AFTER LAST TREATMENT)
Duration of AE	17 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until

second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の頭痛及び意識消失を発現した。関連する病歴は，脳波異常（5 歳頃），一時的な会話不能状態 5 歳頃），選択的緘黙症及び潰瘍性大腸炎であった。被験者は非アルコール摂取者であった。選択的緘黙症及び不安障害のため，被験者はその他の併用療法として精神科治療を長年受けていた。

20[redacted] 年 [redacted] 月 [redacted] 日，頭痛及び意識消失が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，頭痛及び意識消失は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。

退院時要約による情報を以下に記す：被験者は入院する前日に胸骨後方の胸痛を訴え，胸痛は接触時に悪化した。同様の発作は以前にも認められ，その際には数分間持続した。被験者によると，頭痛，悪心，呼吸困難，視覚障害，並びに左側により顕著な顔面及び腕のしびれ感が認められた。身体的診察中には突発性の会話不能状態が発現し，数秒間持続した。筋緊張の低下も伴っていたが，発作はみられなかった。心拍数は不安のため 130 bpm であり，発作中の血圧は 160/120 mmHg，発作後は 150/100 mmHg であった。その他のすべてのパラメータは正常と判断された。20[redacted] 年 [redacted] 月 [redacted] 日，心臓の診察が再度実施され，新たな所見は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者の母親が被験者の周囲とのコミュニケーションの欠如，食物摂取量の少なさ及び離脱行動に懸念を示したことから，精神科医による診察が行われた。被験者は出血発作を減少させるため，食事量を減らしていた。栄養療法のため，小児胃腸科での治療が継続された。その他の検査結果に異常はみられなかった。当時，主訴の身体的原因を排除した後に精神保健クリニックを受診すること及びおそらく精神科へ紹介することも可能であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は内分泌科の診察を受けた。甲状腺の機能は正常であったが，超音波検査で甲状腺肥大が認められた。心臓学的，神経学的及び内分泌学的診断により，被験者の症状の

最終的な原因を説明することは不可能であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者の状態は改善し，退院した。
治療薬として Dexaven（デキサメタゾン），20%マンニトール，Acix（アシクロビル），Ketonal（ケトプロフェン），Midanium（ミダゾラム），Nalpain，Ondansetron accord（オンダンセトロン塩酸塩水和物），Biotaksym（セフォタキシムナトリウム），Penicillinum crystallisatum, Polprazol（オメプラゾール），Relanium（ジアゼパム），Tarcefoksym（セフォタキシムナトリウム），アザチオプリン，Chlorprothixen，5%ブドウ糖，Kabipac，0.9%塩化ナトリウム，Nutridrink，Paracetamol b. braun（アセトアミノフェン），Paracetamol kabi（アセトアミノフェン），ペニシリン及びアセトアミノフェンが投与された。

The patient's past medications include:

VALPROIC ACID for LOSS OF CONTACT (20[redacted] - 20[redacted])

Causality for HUMIRA (Blinded)

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1) Loss of consciousness (10024855) (Loss of consciousness (10024855)) [v.20.1] [10024855]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Headache (10019211) (Headache (10019211)) [v.20.1] [10019211]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of HEADACHES, LOSS OF CONSCIOUSNESS

- Investigator: N/A

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ANA SCREENING TEST: Negative

[redacted] 20[redacted] ANTI-NEURON CELL SURFACE ANTIGEN ANTIBODIES: None

[redacted] 20[redacted] APTT: 20.2 No Unit

[redacted] 20[redacted] APTT: 26.0 No Unit

[redacted] 20[redacted] BASOPHIL: 0.02 X10**3/MCL

[redacted] 20[redacted] BASOPHIL: 0.01 X10**3/MCL

[redacted] 20[redacted] BASOPHIL PERCENTAGE: 0.3 %

[redacted] 20[redacted] BASOPHIL PERCENTAGE: 1 %

[redacted] 20[redacted] BLOOD CULTURE: NEGATIVE

[redacted] 20[redacted] BLOOD PRESSURE (AFTER LOSS OF CONTACT): 150/100 mmHG

[redacted] 20[redacted] BLOOD PRESSURE (DURING LOSS OF CONTACT): 160/120 mmHG

[redacted] 20[redacted] BLOOD-VENOUS-AEROBIC BACTERIA: Negative

[redacted] 20[redacted] BNP: 19.9 PG/ML

[redacted] 20[redacted] BODY WEIGHT: 43 KG

[redacted] 20[redacted] BODY WEIGHT: 43 KG

[redacted] 20[redacted] BODY WEIGHT: 43 KG

[redacted] 20[redacted] CALCIUM: 2.47 MMOL/L

[redacted] 20[redacted] CEREBRAL FLUID CULTURE: NEGATIVE

[redacted] 20[redacted] CEREBROSPINAL FLUID (CSF) ANALYSIS: Appearance l(CSF): colourless, clear, Appearance 2 (CSF): colourless, clear;

[redacted] 20[redacted] CERVICAL SPINE X-RAY (AP AND LATERAL VIEW): Radiologically normal image.

[redacted] 20[redacted] CHEST X-RAY: NORMAL; Lung fields without any focal lesions. No fluid in the pleural cavity. Normal cardiac silhouette. Artifacts in the supraclavicular area on the left.

[redacted] 20[redacted] CK: 36.0 U/L

[redacted] 20[redacted] CREATININE: 0.46 mg/dL

[redacted] 20[redacted] CRP: 0.2 mg/dL

[redacted] 20[redacted] CT SCAN WITHOUT CONTRAST: NORMAL

[redacted] 20[redacted] D-DIMER: 2.84 mg/dL

[redacted] 20[redacted] D-DIMER: 0.79 MG/L

Unknown date ECG (SCREENING): Normal

[redacted] 20[redacted] ECG HOLTER: CONCLUSIONS: Recording appropriate for the age of the patient.

[redacted] 20[redacted] ECHOCARDIOGRAM: CONCLUSION: Normal echocardiogram.

[redacted] 20[redacted] EEG: CONCLUSIONS: Recording of the brain bioelectrical activity when awake is borderline normal.

[redacted] 20[redacted] EEG WITH VISUAL PROVOCATION: CONCLUSIONS: Recording of the brain bioelectrical activity when awake is borderline normal.

[redacted] 20[redacted] ELECTROCARDIOGRAM: Normal

[redacted] 20[redacted] EOSINOPHIL: 0.02 X10**3/MCL

[redacted] 20[redacted] EOSINOPHIL PERCENTAGE: 0.3 %

[redacted] 20[redacted] EOSINOPHIL PERCENTAGE: 0.3 %

[redacted] 20[redacted] ERYTHROCYTES (CSF): 1 MCL

[redacted] 20[redacted] FE: 28 MCG/DL

[redacted] 20[redacted] GLUCOSE: 118 mg/dL

[redacted] 20[redacted] GLUCOSE: 119 mg/dL

[redacted] 20[redacted] GLUCOSE (CSF): 58 mg/dL

[redacted] 20[redacted] HCT: 35.2 %

[redacted] 20[redacted] HCT: 32.3 %

[redacted] 20[redacted] HCT: 33.5 %

[redacted] 20[redacted] HCT: 33.6 %

[redacted] 20[redacted] HEART RATE: 130 BPM

[redacted] 20[redacted] HEMOGLOBIN: 11 G/DL

[redacted] 20[redacted] HGB: 11.0 G/DL

[redacted] 20[redacted] HGB: 10.8 G/DL

[redacted] 20[redacted] HGB: 10.4 G/DL

[redacted] 20[redacted] HGB: 10.9 G/DL

[redacted] 20[redacted] INR: 1.09 No Unit

[redacted] 20[redacted] INR: 1.14 No Unit

[redacted] 20[redacted] IONIZED CALCIUM: 1.09 MMOL/L

[redacted] 20[redacted] LEUCOCYTES (CSF): 1 MCL

[redacted] 20[redacted] LYMPHOCYTE: 1.25 X10**3/MCL

[redacted] 20[redacted] LYMPHOCYTE: 20.7 %

[redacted] 20[redacted] LYMPHOCYTE: 1.45 X10**3/MCL

[redacted] 20[redacted] LYMPHOCYTE PERCENTAGE: 18.9 %

[redacted] 20[redacted] MAGNESIUM: 19.4 MG/L

[redacted] 20[redacted] MCH: 30.6 PG

[redacted] 20[redacted] MCH: 30.6 PG

[redacted] 20[redacted] MCH: 30.9 PG

[redacted] 20[redacted] MCH: 30.2 PG

[redacted] 20[redacted] MCHC: 31.3 G/DL

[redacted] 20[redacted] MCHC: 33.4 G/DL

[redacted] 20[redacted] MCHC: 31 .0 G/DL

[redacted] 20[redacted] MCHC: 32.4 G/DL

[redacted] 20[redacted] MCV: 98.1 FL

[redacted] 20[redacted] MCV: 91.5 FL

[redacted] 20[redacted] MCV: 99.4 FL

[redacted] 20[redacted] MCV: 93.1 FL

[redacted] 20[redacted] MENINGITIS PANEL: Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenza (CSF): negative

[redacted] 20[redacted] MENINGITIS PANEL 9: CMV, EBY, adenovirus, HSY type 1 and 2, VZV, enterovirus, parechovirus, HHV type 6 and 7, parvovirus B19 (CSF): negative;

[redacted] 20[redacted] MONOCYTE: 0.50 X10**3/MCL

[redacted] 20[redacted] MONOCYTE: 8.1 %

[redacted] 20[redacted] MONOCYTE: 0.57 X10**3/MCL

[redacted] 20[redacted] MONOCYTE PERCENTAGE: 7.6 %

[redacted] 20[redacted] MPV: 10.40 FL

[redacted] 20[redacted] MPV: 10.5 FL

[redacted] 20[redacted] MPV: 9.90 FL

[redacted] 20[redacted] MPV: 10.2 FL

[redacted] 20[redacted] MRI: CNS-NORMAL

[redacted] 20[redacted] NEUTROPHIL: 72.9 %

[redacted] 20[redacted] NEUTROPHIL: 4.82 X10**3/MCL

[redacted] 20[redacted] NEUTROPHIL: 4.97 X10**3/MCL

[redacted] 20[redacted] NEUTROPHIL PERCENTAGE: 70.8 %

[redacted] 20[redacted] PDW: 10.2 FL

[redacted] 20[redacted] PLATELET COUNT: 431 X10**3/MCL

[redacted] 20[redacted] PLT: 460 X10**3/MCL

[redacted] 20[redacted] PLT: 368 X10**3/MCL

[redacted] 20[redacted] PLT: 371 X10**3/MCL

[redacted] 20[redacted] POTASSIUM: 3.54 MMOL/L

[redacted] 20[redacted] PROTEIN: 6.63 G/DL

[redacted] 20[redacted] PROTEIN (CSF): 34 mg/dL

[redacted] 20[redacted] PT: 12.0 No Unit

[redacted] 20[redacted] PT: 12.5 No Unit

[redacted] 20[redacted] RBC: 3.59 X10**6/MCL

[redacted] 20[redacted] RBC: 3.53 X10**6/MCL

[redacted] 20[redacted] RBC: 3.37 X10**6/MCL

[redacted] 20[redacted] RBC: 3.61 X10**6/MCL

[redacted] 20[redacted] RDW-CV: 16.5 %

[redacted] 20[redacted] RDW-CV: 16.2 %

[redacted] 20[redacted] RDW-CV: 15.9 %

[redacted] 20[redacted] RDW-SD: 56.6 FL

[redacted] 20[redacted] RDW-SD: 50.5 FL

[redacted] 20[redacted] SERUM ALT: 10 IU/L

[redacted] 20[redacted] SERUM AST: 27 IU/L

[redacted] 20[redacted] SERUM CA: 2.47 MMOL/L

[redacted] 20[redacted] SERUM CA: 2.33 MMOL/L

[redacted] 20[redacted] SERUM CREATININE: 0.46 mg/dL

[redacted] 20[redacted] SERUM GLUCOSE: 90 mg/dL

[redacted] 20[redacted] SERUM K: 3.54 MMOL/L

[redacted] 20[redacted] SERUM MG: 19.1 MG/L

[redacted] 20[redacted] SERUM NA: 139 MMOL/L

[redacted] 20[redacted] SERUM UREA: 24 mg/dL

[redacted] 20[redacted] SGOT/AST: 27 IU/L

[redacted] 20[redacted] SGPT/ALT: 10 IU/L

[redacted] 20[redacted] SODIUM: 139 MMOL/L

[redacted] 20[redacted] TIBC: 317 MCG/DL

[redacted] 20[redacted] TOTAL PROTEIN: 7.04 G/DL

[redacted] 20[redacted] TROPONIN I: <5 NG/L

[redacted] 20[redacted] TSH U: 0.431 IU/mL

Unknown date ULTRASOUND OF THYROID (DURING HOSPITALIZATION): Enlarged thyroid, slightly hypoechoic, mostly peripherally, heterogenic, no focal lesions. Right lobe: 17.1 x 17.5 mm Left lobe: 15.9 x 14.4

[redacted] 20[redacted] URIC ACID: 24 mg/dL

[redacted] 20[redacted] WBC: 6.64 X10**3/MCL

[redacted] 20[redacted] WBC: 6.61 X10**3/MCL

[redacted] 20[redacted] WBC: 6.62 X10**3/MCL

[redacted] 20[redacted] WBC: 7.02 X10**3/MCL

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD	1[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: CAMPYLOBACTER INFECTION	20[redacted]
OTHER: CLOSTRIDIUM DIFF. INFECTION	20[redacted]
Ulcerative colitis	20[redacted]
ANEMIA: ANEMIA	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 15	28

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -138
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -99
FERRIC HYDROXIDE POLYMALTOSE COMPLEX	1 DF (dosage form)	QD	Y-M: 20[redacted] / -32
DICLOFENAC POTASSIUM	1 TABLET	QD	Y-M: 20[redacted] / -28
LEKOVIT CA	1 TABLET	QD	Y-M: 20[redacted] / -28
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -28

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -138	Y-M: 20[redacted] / 29
FERRIC HYDROXIDE POLYMALTOSE COMPLEX	1 DF (dosage form)	QD	Y-M: 20[redacted] / -32	Y-M: 20[redacted] / 15
DICLOFENAC POTASSIUM	1 TABLET	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / 18
LEKOVIT CA	1 TABLET	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / 18
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / 24
AKRITOIN	100 mg (milligram(s))	TID	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 7
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 8	Y-M: 20[redacted] / 18
FERROUS TARTRATE	1 DF (dosage form)	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 18
BLOOD AND RELATED PRODUCTS	2 DF (dosage form)	QD	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
DEXTROSE AND SODIUM CHLORIDE INJECTION	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
PARACETAMOL	1 g (gram(s))	QD	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
CEFTAZIDIME	2 g (gram(s))	TID	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 29
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 21
CALCIUM	10 mL (millilitre(s))	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] /

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
			20	91
DEXTROSE AND SODIUM CHLORIDE INJECTION	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 23
BLOOD AND RELATED PRODUCTS	2 DF (dosage form)	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
HYDROCORTISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
IBUPROFEN	400 mg (milligram(s))	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
PARACETAMOL	1 g (gram(s))	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 29
HYDROCORTISONE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 24
OSMOTAN	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 27
POTASSIUM CHLORIDE	1 TABLET	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 29
HYDROCORTISONE	50 mg (milligram(s))	TID	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 29
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted] / 30	ONGOING
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / 30	ONGOING
PREDNISONE	20+10 mg (milligram(s))	BID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 50
FERROUS TARTRATE	1 DF (dosage form)	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 91
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 91
POTASSIUM CHLORIDE	1 TABLET	BID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 91
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 60
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 70
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 80

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
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 91

Event #1: Serious Adverse Event

Event Description	WORSENING OF ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 18 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	

[redacted]20[redacted] (RX DAY 19): BLOOD TRANSFUSION: ANEMIA PARTIALLY RESOLVED. NO ADVERSE EVENTS WERE OBSERVED DURING AND AFTER TRANSFUSION.; [redacted]20[redacted] (RX DAY 21): ECG: SINUS RHYTHM 100 PER MINUTE, PR INTERVAL, QTC, QTC COMPLEX, ARE NORMAL, T - WAVES ARE FLAT (NO DEPRESSIONS, NO INVERSIONS, NO ELEVATIONS)

AE Stopped Rx Day	91 (76 DAYS AFTER LAST TREATMENT)
Duration of AE	74 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INTESTINAL BLEEDING
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 19 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	

NOT APPLICABLE	
AE Stopped Rx Day	31 (16 DAYS AFTER LAST TREATMENT)
Duration of AE	13 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

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

Event Description	PERICARDITIS
Preferred term	心膜炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 21 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	29 (14 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and
Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum

dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の心膜炎及び貧血の悪化が認められた。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。

本試験では，最初の 8 週間はすべての被験者がアダリムマブの投与を受けることとしていたが，当該被験者は投与 2 週時まで盲検下でアダリムマブの投与を受けた。

20[redacted] 年 [redacted] 月 [redacted] 日のスクリーニング時に貧血が認められた（臨床検査値は報告されず）。

20[redacted] 年 [redacted] 月 [redacted] 日，貧血の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，心膜炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，心膜炎は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血の悪化は回復した。

咽喉痛，貧血及び C 反応性たん白濃度の著しい上昇の徴候及び症状がみられた。C 反応性たん白高値は当初 20[redacted] 年 [redacted] 月 [redacted] 日のベースライン時に認められていた。

20[redacted] 年 [redacted] 月 [redacted] 日，臨床検査の結果，ヘモグロビン低値及び C 反応性たん白高値の持続がみられた。治験責任医師は，被験者の両親に連絡を取り，輸血，並びに感染原因及び感染源の評価のため被験者を入院させることを提案した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は心膜炎と診断された。

胸痛，頻脈，全身倦怠及び C 反応性たん白濃度高値が認められた。心エコー検査により心膜炎と診断され（心嚢液），静脈内ステロイド及びセフタジジムの経験的投与が行われた。心膜炎の正確な原因は不明であったが，一つの可能性としてアダリムマブの副作用が挙げられた。血清学的検査の結果はすべて陰性であった。心膜炎は，静脈内ステロイド療法の開始後に迅速に回復した。貧血は，血液 4 単位の輸血後にある程度回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

本事象に関連したリスク因子には，潰瘍性大腸炎及びアダリムマブ投与があった。

治療薬として Ferroplex，オメプラゾール，アザチオプリン，ヒドロコルチゾン，Kalipoz，イブプロフェン，Encorton，アセトアミノフェン及びブドウ糖／塩化ナトリウムが投与され，輸血が行われた。

Causality for HUMIRA (Open Label)

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1) Pericarditis (10034484) (Pericarditis (10034484)) [v.21.0] [10034484]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Yes

2) Anemia aggravated (10054309) (Anaemia (10002034)) [v.21.0] [10054309]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Alternative Etiology for HUMIRA (Open Label)

Event of PERICARDITIS

- Investigator: N/A

- AbbVie: N/A

Event of WORSENING OF ANEMIA

- Investigator: Intestinal bleeding

- AbbVie: A common complication of UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CRP: Elevated, 200 mg/dl

[redacted] 20[redacted] ECG: RMZ 100 / MIN, Q, QTC, QRS - IN NORM THREATS T PLAYED

[redacted] 20[redacted] Electrocardiogram: Not clinical significant-abnormal T waves

[redacted] 20[redacted] Hemoglobin: 6.0 G/DL (normal 11.0 to 14.3)

[redacted] 20[redacted] HEMOGLOBIN: 9.2 G/DL (normal 11.0 to 14.3)

[redacted] 20[redacted] High-sensitivity C-reactive protein: 196.8 MG/L (normal 0 to 5)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
手首関節骨折	X			

Treatment Group	Age at Study Start	Sex	Race
IHD-MHD	[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: HB 7.3G/DL	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: POSITIVE QUANTIFERON TEST	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	55
MHD	[redacted]20[redacted] / 56	[redacted]20[redacted] / 357	309

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -220
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -161
CALCIUM	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14
COLECALCIFEROL	2 gtt (drop(s))	QD	Y-M: 20[redacted] / -14
ISONIAZID	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
POTASSIUM	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
SUCCIFER	5 mL (millilitre(s))	BID	Y-M: 20[redacted] / -14
VIGRAN	1 TABLET	QD	Y-M: 20[redacted] / -14

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -220	ONGOING
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -161	Y-M: 20[redacted] / 127
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 29
CALCIUM	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 36
COLECALCIFEROL	2 gtt (drop(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 36
POTASSIUM	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 36
SUCCIFER	5 mL (millilitre(s))	BID	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 73
ISONIAZID	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 127
VIGRAN	1 TABLET	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 127
PARACETAMOL	200 mg (milligram(s))	QD	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 10

Event #1: Serious Adverse Event

Event Description	WRIST FRACTURE LEFT
Preferred term	手首関節骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 10
Age at AE Onset	[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 10): X-RAY: HAND WRIST FRACTURE LEFT; PLASTER DRESSING: PLASTER WAS REMOVED ON [redacted]20[redacted].	
AE Stopped Rx Day	29
Duration of AE	20 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MECHANICAL INJURY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	PERSIST OR SIGNIF DISABILITY/INCAPACITY, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and
Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum
dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching
placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg
(maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit

and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，[redacted] 歳の男児（ポーランド）であり，重篤な有害事象の左手首関節骨折を発現した。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，左手首関節骨折が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左手首関節骨折は回復した。
被験者は階段から転落した。手の X 線検査の結果，手根骨骨折が認められ，ドレッシングプラスターによる固定が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，プラスターを除去した。
治療薬としてアセトアミノフェンが投与された。

Causality for HUMIRA (Blinded)

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1) Wrist fracture (10048049) (Wrist fracture (10048049)) [v.21.0] [10048049]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of WRIST FRACTURE LEFT

- Investigator: Mechanical injury.

- AbbVie: A Trauma.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] X-RAY: Hand wrist fracture left.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]
OTHER: NAUSEA AND VOMITING WHEN PATIENT GOES TO TOILET	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -168
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -82
HYDROCORTISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -33
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / -17

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / -17	Y-M: 20[redacted] / 28
METHYLPREDNISOLONE	8 mg (milligram(s))	QD	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 35
METHYLPREDNISOLONE	6 mg (milligram(s))	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 42
METHYLPREDNISOLONE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 49
METHYLPREDNISOLONE	2 mg (milligram(s))	QD	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 57
ADALIMUMAB	40 mg (milligram(s))	OTHER: EVERY WEEK	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 111
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 71
METHYLPREDNISOLONE	24 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 111
NADROPARIN CALCIUM	5700 IU (international unit(s))	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 177
ALPRAZOLAM	0.5 mg (milligram(s))	BID	Y-M: 20[redacted] / 111	Y-M: 20[redacted] / 113
CEFUROXIME	1.5 g (gram(s))	BID	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 113
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 113
NAPROXEN	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 115

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
ALIZAPRIDE	50 mg (milligram(s))	QID	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 122
NADROPARIN CALCIUM	2850 IU (international unit(s))	QD	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 122
RANITIDINE HYDROCHLORIDE	50 mg (milligram(s))	TID	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 130
TRAMADOL HYDROCHLORIDE	50 mg (milligram(s))	QID	Y-M: 20[redacted] / 115	Y-M: 20[redacted] / 122

Event #1: Serious Adverse Event

Event Description	WORSENING ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 38
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 112): TOTAL COLOPROCTECTOMY BY SINGLE INCISION LAPAROSCOPIC SURGERY: REMISSION OF ULCERATIVE COLITIS

AE Stopped Rx Day	274 (232 DAYS AFTER LAST TREATMENT)
Duration of AE	237 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	STUDY DISEASE RELATED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.

IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted]20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女性（ベルギー）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（汎大腸炎）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。薬剤投与により潰瘍性大腸炎の症状（排便回数増加及び血便）に改善が認められなかったことから，手術が予定された。20[redacted] 年 [redacted] 月 [redacted] 日，単孔式腹腔鏡下手術により結腸直腸全摘除が行われた。腹壁の術後（静脈）血栓症が認められ，Fraxiparin（ヘパリンカルシウム）が投与された。術後の悪心及び嘔吐はコルチコイドの投与により回復した。潰瘍性大腸炎は寛解となった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてラニチジン，Fraxiparine（ヘパリンカルシウム），Xanax（アルプラゾラム），Litican，Motilum（ドンペリドン），Dipidolor，アセトアミノフェン，Dafalgan（アセトアミノフェン），Tradonal（トラマドール塩酸塩），Zantac（ラニチジン塩酸塩），Taradyl，Naprosyne（ナプロキセン），Zinacef（セフロキシム），メトロニダゾール，Primperan（メトクロプラミド），Catapressan（クロニジン塩酸塩），オンダンセトロン，Solu-medrol（メチルプレドニゾロンコハク酸エステルナトリウム）及び Solu-cortef（ヒドロコルチゾンコハク酸エステルナトリウム）が投与された。

The patient's past medications include:

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

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

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

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

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING ULCERATIVE COLITIS

- Investigator: Study disease related

- AbbVie: The underlying UC

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Colonoscopy: Rectum, sigmoid, Descending/Transverse colon - 3 (Severe disease - spontaneous bleeding, ulceration). Ascending colon/cecum (Moderated disease - marked erythema, absent vascular pattern, friability, erosions).

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD-MSD-FNREIND	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: IBD	20[redacted]
Ulcerative colitis	20[redacted]
OSTEOPENIA: BONE DENSITY DECREASE (DENSITOMETRY)	20[redacted]
ANEMIA: SIDEROPENIC	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 45	58
MSD	[redacted]20[redacted] / 60	[redacted]20[redacted] / 262	214
FNREIND	[redacted]20[redacted] / 274	[redacted]20[redacted] / 360	94

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -290
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -290
ESCHERICHIA COLI	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -245
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -245
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -245
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -121
CITRIC ACID	18.0 g (gram(s))	BID	Y-M: 20[redacted] / -40
MAGNESIUM OXIDUM LEVE	3.5 g (gram(s))	BID	Y-M: 20[redacted] / -40
SODIUM PICOSULFATE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -40

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
ESCHERICHIA COLI	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -245	ONGOING
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -245	ONGOING
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -245	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -121	ONGOING
PARACETAMOL	250 mg (milligram(s))	OTHER: [redacted].20[redacted] 250 MG [redacted].20[redacted] 500 MG [redacted].20[redacted] 250 MG	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 336
HYLAK	40 gtt (drop(s))	OTHER: [redacted].20[redacted] [redacted].20[redacted]	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 223
PARACETAMOL	400 mg (milligram(s))	QID	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 238
CIPROFLOXACIN HYDROCHLORIDE	200 mg (milligram(s))	BID	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 243
METRONIDAZOLE	430 mg (milligram(s))	TID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 242
PREDNISONE	15 mg (milligram(s))	BID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 256
OMEPRAZOLE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 270
CIPROFLOXACIN	250 mg (milligram(s))	BID	Y-M: 20[redacted]	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
HYDROCHLORIDE			[redacted] / 243	/ 248
METRONIDAZOLE	250 mg (milligram(s))	BID	Y-M: 20[redacted]- [redacted] / 243	Y-M: 20[redacted]- [redacted] / 248
FLUCONAZOLE	100 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 243	Y-M: 20[redacted]- [redacted] / 270
PREDNISONE	12.5 mg (milligram(s))	BID	Y-M: 20[redacted]- [redacted] / 257	Y-M: 20[redacted]- [redacted] / 261
METHYLPREDNISOLONE SODIUM SUCCINATE	250 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 262	Y-M: 20[redacted]- [redacted] / 262
METHYLPREDNISOLONE SODIUM SUCCINATE	40 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 263	Y-M: 20[redacted]- [redacted] / 264
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 265	Y-M: 20[redacted]- [redacted] / 297
CITRIC ACID	18 g (gram(s))	BID	Y-M: 20[redacted]- [redacted] / 269	Y-M: 20[redacted]- [redacted] / 269
MAGNESIUM OXIDUM LEVE	3.5 g (gram(s))	BID	Y-M: 20[redacted]- [redacted] / 269	Y-M: 20[redacted]- [redacted] / 269
SODIUM PICOSULFATE	10 mg (milligram(s))	BID	Y-M: 20[redacted]- [redacted] / 269	Y-M: 20[redacted]- [redacted] / 269

Event #1: Serious Adverse Event

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 235
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 235): Blood BLOOD CULTURE:; Other SWAB SWAB FROM THE TONSILS: POSITIVE-STREPTOCOCCUS VIRIDANS HAEMOPHILUS PARAINFLUENZAE; Other SWAB NASAL SWAB:; Other STOOL RECTAL SWAB: POSITIVE-ENTEROCOCCUS SPECIES; Urine AEROBIC CULTIVATION:

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 235): CHEST X-RAY: NO PATHOLOGICAL CHANGES

AE Stopped Rx Day	243
Duration of AE	9 DAYS
Severity	MODERATE

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

Event #2: Serious Adverse Event

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 269
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 238): S_FERI: 531.24 [15 - 150] MCG/ML; [redacted]20[redacted] (RX DAY 269): FE_S: 4.9 [9 - 21.5] MCMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 269): Other SWAB FROM THE TONSILS SWAB FROM THE TONSILS: POSITIVE-ENTEROBACTER CLOACAE GROUP ++

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 270): RECTOSIGMOIDOSKOPY: UC, MAYO ENDOSCOPIC SCORE 3

AE Stopped Rx Day	277
Duration of AE	9 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and
Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum
dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching
placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg
(maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.

MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（スロバキア共和国）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な有害事象の急性鼻咽喉炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，発熱，疲労，体重減少，腹痛及び血便の徴候及び症状のため入院し，薬剤が投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてメトロニダゾール，Entizol（メトロニダゾール），Diflucan（フルコナゾール），prednisone，Helicid（オメプラゾール），Ciprinol（シプロフロキサシン塩酸塩水和物），Perfalgan（アセトアミノフェン）及び Medociprin（シプロフロキサシン塩酸塩水和物）が投与さ

れた。

The patient's past medications include:

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

Causality for HUMIRA (Blinded)

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1)　UC aggravated (10045283)　(Colitis ulcerative (10009900))　[v.18.0]　[10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of UC FLARE

- Investigator: Colitis ulcerosa flare

- AbbVie: The underlying disorder UC

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] hemoglobin: 108 G/L (normal 110 to 150)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（スロバキア共和国）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，コルチコステロイド抵抗性の潰瘍性大腸炎再燃の徴候が持続していたため，被験者は入院した。潰瘍性大腸炎の再燃に伴う徴候及び症状として，発熱，体重減少，血便，頻回の排便及び炎症活性の増強が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として prednisone が投与された。

The patient'spast medications include:

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

HYLAK for DIARRHEA ([redacted] 20[redacted] - [redacted] 20[redacted])

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

SOLUMEDROL for ULCERATIVE COLITIS FLARE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.19.1] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Alternative Etiology for HUMIRA (Open Label)

Event of UC FLARE

- Investigator: ULCERATIVE COLITIS.

- AbbVie: THE UNDERLYING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] RBC: 3.39 X10**12/L (normal 3.80 to 5.20)

[redacted] 20[redacted] FE-S: 531.24 MCG/ML (normal 15 to 150.0)

[redacted] 20[redacted] C-reactive protein: 56.1 MG/L (normal 0 to 5)

[redacted] 20[redacted] FE-S: 4.9 MCMOL/L (normal 9.0 to 21.5)

[redacted] 20[redacted] WBC: 3.30 X10**9/L (normal 4.00 to 12.00)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHD-MHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
Ulcerative colitis	20[redacted]
SCOLIOSIS: ADOLESCENT IDIOPATHIC SCOLIOSIS	20[redacted]
ANEMIA: SIDEROPENIC	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MHD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	310

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -254
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -254
OMEPRAZOLE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / -103
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -103
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -70
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -70
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -70
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -40
CITRIC ACID	18.0 g (gram(s))	BID	Y-M: 20[redacted] / -21
MAGNESIUM OXIDUM LEVE	3.5 g (gram(s))	BID	Y-M: 20[redacted] / -21
SODIUM PICOSULFATE	10.0 mg (milligram(s))	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
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -254	ONGOING
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -70	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -40	ONGOING
PARACETAMOL	500 mg (milligram(s))	OTHER: [redacted]	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 211
PARACETAMOL	630 mg (milligram(s))	QID	Y-M: 20[redacted] / 190	Y-M: 20[redacted] / 192
AUGMENTIN	1.2 g (gram(s))	TID	Y-M: 20[redacted] / 190	Y-M: 20[redacted] / 195
AUGMENTIN	375 mg (milligram(s))	TID	Y-M: 20[redacted] / 195	Y-M: 20[redacted] / 201

Event #1: Serious Adverse Event

Event Description	PHARYNGITIS ACUTA
Preferred term	咽頭炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 190
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 191): Other NASAL SWAB AEROBIC CULTIVATION:; Stool AEROBIC CULTIVATION:; Other SWAB FROM THE TONSILS AEROBIC CULTIVATION: POSITIVE-STREPTOCOCCUS ANGINOSUS +; Urine AEROBIC CULTIVATION:

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 190): ULTRASOUND EXAMINATION: WITHOUT PATHOLOGICAL FINDINGS

AE Stopped Rx Day	195
Duration of AE	6 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until

second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女性（スロバキア共和国）であり，重篤な有害事象の急性咽頭炎を発現した。関連する病歴は，潰瘍性大腸炎，潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎）及び鉄欠乏性貧血であった。

20[redacted] 年 [redacted] 月 [redacted] 日，急性咽頭炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性咽頭炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，体の痛み，全身脱力，最高体温 39°C，乾性咳嗽，咽喉痛，食欲減退及び打診音の異常が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，診断及び治療のため，被験者は救急病院に入院した。入院時，気道感染及び脱水の臨床徴候がみられたが，神経学的所見は正常であった。治療として Augmentin（アモキシシリン／クラブラン酸）及び Perfalgan（アセトアミノフェン）の投与，非経口的水分補給，並びに対症療法が開始された。入院当初は発熱が認められたがその後解熱し，排便は 1 日 1 回，食事に耐性もみられ，問題はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師によると，被験者には本事象に関連したリスク因子はなかった。

治療薬として Perfalgan（アセトアミノフェン）及び Augmentin（アモキシシリン／クラブラン酸）が投与された。

The patient's past medications include:

OMEPRAZOL for COMBINED TREATMENT WITH PREDNISON ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISON for DISEASE ACTIVATION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1)　Acute pharyngitis (10001002)　(Pharyngitis (10034835))　[v.20.0]　[10001002]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of PHARYNGITIS ACUTE

- Investigator: Ulcerative colitis

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Hemoglobin: 125 G/L (normal 120 to 155)

[redacted] 20[redacted] Nasal swab (aerobic cultivation): Negative

[redacted] 20[redacted] STOOL (aerobic cultivation): Negative

[redacted] 20[redacted] Swab from the tonsils (Aerobic cultivation): Positive(streptococcus anginosus)

[redacted] 20[redacted] Ultrasound examination: Without pathological findings

[redacted] 20[redacted] Urine (aerobic cultivation): Negative

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ISD-MHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MHD	[redacted]20[redacted] / 60	[redacted]20[redacted] / 120	74

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -120

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 68
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 64
NUTRIENTS NOS	200 mcL (microlitre(s))	BID	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 64
ONDANSETRON	50 mg (milligram(s))	PRN	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 64

Event #1: Serious Adverse Event

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 52
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 59): CRP: 49 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 59): Stool STOOL MICROBIOLOGY: -NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 72): SIGMOIDESCOPY: SICK COLON MUCOSA SARTING DEPTH OF 30 CM. POSITIVE COLON COLITIS/BLEEDING.

AE Stopped Rx Day	64
Duration of AE	13 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DISEASE FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,

MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女性（イスラエル）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，潰瘍性大腸炎（左側）であった。
20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な有害事象の発熱が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な有害事象の体重減少が発現し，持続していた。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，下痢が発現し，治験薬の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，疾患の再燃のため被験者は入院し，発熱及び下痢の持続と共に，非重篤な有害事象の疲労，悪心及び嘔吐の症状が認められた。併用薬が投与された。20[redacted] 年 [redacted] 月 [redacted] 日，治験薬の投与が再開されたが，非反応であったため，投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，悪心，嘔吐及び疲労は回復し，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，発熱は回復した。
治療薬としてアセトアミノフェン，Zofran（オンダンセトロン塩酸塩水和物），Peptamen 及び Flagyl（メトロニダゾール）が投与された。

The patient's past medications include:

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

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

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.21.0] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of UC FLARE

- Investigator: Disease flare.

- AbbVie: The underlying disorder Ulcerative Colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CRP: 49 MG/L (normal 0 to 5)

[redacted] 20[redacted] SIGMOIDOSCOPY: Sick colon mucosa starting depth of 30 cm. Positive colon colitis/bleeding.

[redacted] 20[redacted] STOOL MICROBIOLOGY: Negative

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
IHDOL-MHD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: MALNUTRITION	NOT REPORTED
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
FLEXIBLE SIGMOIDOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHDOL	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	56
MHD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 267	224

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -129
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -127
AZATHIOPRINE	75 mg (milligram(s))	QD	Y-M: 20[redacted] / -47
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -47
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -47
IMIPENEM	500 mg (milligram(s))	QID	Y-M: 20[redacted] / -40
METRONIDAZOLE	250 mg (milligram(s))	TID	Y-M: 20[redacted] / -40

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -127	ONGOING
AZATHIOPRINE	75 mg (milligram(s))	QD	Y-M: 20[redacted] / -47	ONGOING
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 50
CEFUROXIME	750 mg (milligram(s))	TID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 71
SACCHAROMYCES BOULARDII	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 76
IBUPROFEN	200 mg (milligram(s))	QD	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 69
PARACETAMOL	500 mg (milligram(s))	OTHER: WHEN NEEDED	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 71
AMIKACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 75
BUDESONIDE	500 mcg (microgram(s))	BID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 76
ENOXAPARIN SODIUM	33 mg (milligram(s))	QD	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 78
CEFTRIAXONE SODIUM	2 g (gram(s))	BID	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 78
HYDROXYZINE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 78
CLEMASTINE FUMARATE	1 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 79
NAPROXEN	125 mg (milligram(s))	BID	Y-M: 20[redacted] /	Y-M: 20[redacted] / 79

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ALBUMIN HUMAN	50 mL (millilitre(s))	QD	71 Y-M: 20[redacted] / 73	Y-M: 20[redacted] / 77
PHYTOMENADIONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 75

Event #1: Serious Adverse Event

Event Description	ERYTHREMA NODOSUM
Preferred term	結節性紅斑
AE Onset Date / Rx Day	[redacted]20[redacted] / 65
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	79
Duration of AE	15 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ERYTHEMA NODOSUM MIGHT HAVE OCCURRED DUE TO URINARY TRACT INFECTION IN PERSON WITH CU
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	URINAL TRACT INFECTION
Preferred term	尿路感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 65
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	

SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	72
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THAT WAS URINARY TRACT INFECTION, THERE WAS NO CAUSE FOUND.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
FREIND = 1ST DISEASE FLARE WITH RE-INDUCTION DOSE.
IHD/IHDOL = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
MHD = 0.6 mg/kg (maximum dose of 40 mg) every week.
MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
MPL = Placebo every week.
FNRIEND = for MSD/MPL 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
FRIEND = for MSD/MPL 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every other week (until second disease flare as applicable).
FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second

disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted]20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の女児（ポーランド）であり，重篤な有害事象の尿路感染及び結節性紅斑を発現した。
20[redacted] 年 [redacted] 月 [redacted] 日，尿路感染及び結節性紅斑が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，尿路感染は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，結節性紅斑は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は尿路感染の疑いのため入院した。身体的診察において，両下肢に結節性紅斑が認められた。排尿時の不快感及び両下肢の結節性紅斑を含む徴候及び症状がみられ，抗生剤が投与された。
治療薬として，Zinacef（セフロキシム），Nurofen（イブプロフェン），アセトアミノフェン，アミカシン，Clexane（エノキサパリンナトリウム），ヒドロキシジン，Biotraxon（セフトリアキソンナトリウム水和物），ナプロキセン，20%アルブミン，Clemastin（クレマスチンフマル酸塩），Enterol 及び Zinnat（セフロキシム　アキセチル）が投与された。

The patient's past medications include:

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

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

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

Causality for HUMIRA (Blinded)

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1) Urinary tract infection (10046571) (Urinary tract infection (10046571)) [v.22.0] [10046571]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

2) Erythema nodosum (10015226) (Erythema nodosum (10015226)) [v.22.0] [10015226]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of URINAL TRACT INFECTION

- Investigator: THAT WAS URINARY TRACT INFECTION, THERE WAS NO CAUSE FOUND.

- AbbVie: Not Applicable.

Event of ERYTHREMA NODOSUM

- Investigator: ERYTHEMA NODOSUM MIGHT HAVE OCCURRED DUE TO URINARY TRACT INFECTION IN PERSON WITH UC.

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
感染性腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
IHD-MSD-FREIND	1[redacted]	MALE	ASIAN

Medical History	Onset Year
MIGRAINE HEADACHE: MIGRAINE HEADACHE	NOT REPORTED
OTHER: ACNE VULGARIS	NOT REPORTED
OTHER: CHRONIC RHINITIS	NOT REPORTED
OTHER: DIARRHEA	NOT REPORTED
OTHER: RIGHT COXITIS	NOT REPORTED
Ulcerative colitis	20[redacted]
OTHER: UPPER RESPIRATORY TRACT INFECTION	20[redacted]

Prior Procedures	Procedure Year
COLONOSCOPY: ENDOSCOPY	NOT REPORTED
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD	[redacted] / 1	[redacted] / 43	56
MSD	[redacted] / 57	[redacted] / 113	63
FREIND	[redacted] / 120	[redacted] / 197	87
2nd FLARE OL ADA	[redacted] / 207	[redacted] / 355	158

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -338
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -253
CLOSTRIDIUM BUTYRICUM	2 TABLET	BID	Y-M: 20[redacted] / -112
PRANLUKAST	225 mg (milligram(s))	BID	Y-M: 20[redacted] / -112
ALFACALCIDOL	0.5 mcg (microgram(s))	QD	Y-M: 20[redacted] / -100
FAMOTIDINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -100
MESALAZINE	2000-1600 mg (milligram(s))	BID	Y-M: 20[redacted] / -100
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -99
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -85
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -69
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -55
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -36
PREDNISOLONE	3 mg (milligram(s))	QD	Y-M: 20[redacted] / -22
CARBOCISTEINE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / -6
CLARITHROMYCIN	200 mg (milligram(s))	BID	Y-M: 20[redacted] / -6
DEQUALINIUM CHLORIDE	0.25 mg (milligram(s))	PRN	Y-M: 20[redacted] / -6
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL (millilitre(s))	TID	Y-M: 20[redacted] / -2
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL (millilitre(s))	BID	Y-M: 20[redacted] / -1

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -253	ONGOING
CLOSTRIDIUM BUTYRICUM	2 TABLET	BID	Y-M: 20[redacted] / -112	ONGOING
PRANLUKAST	225 mg (milligram(s))	BID	Y-M: 20[redacted] / -112	ONGOING
MESALAZINE	2000-1600 mg (milligram(s))	BID	Y-M: 20[redacted] / -100	ONGOING
ALFACALCIDOL	0.5 mcg (microgram(s))	QD	Y-M: 20[redacted] / -100	Y-M: 20[redacted] / 71
FAMOTIDINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -100	Y-M: 20[redacted] / 71
PARACETAMOL	400 mg (milligram(s))	PRN	Y-M: 20[redacted] / 38	ONGOING
PREDNISOLONE	1 mg (milligram(s))	QD	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 71
FOSFOMYCIN CALCIUM	1000 mg (milligram(s))	TID	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 89

Event #1: Serious Adverse Event

Event Description	ENTERITIS INFECTIOUS
Preferred term	感染性腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 88): ESR1H: 24.0 [2 - 10] MM

Microbiology

[redacted]20[redacted] (RX DAY 88): Other NASAL MUCOUS MEMBRANE INFLUENZA:

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	90
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ACCIDENTAL EVENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

NOTE: ISD = INDUCTION STANDARD DOSE GROUP, IHD = INDUCTION HIGH DOSE GROUP,
IHDOL = INDUCTION HIGH DOSE OPEN-LABEL GROUP,
MPL = MAINTENANCE PLACEBO GROUP, MSD = MAINTENANCE STANDARD DOSE GROUP,
MHD = MAINTENANCE HIGH DOSE GROUP,
FNREIND = 1ST DISEASE FLARE WITHOUT RE-INDUCTION DOSE,
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ISD = Adalimumab 2.4 mg/kg (maximum dose of 160 mg) at Baseline and matching placebo at Week 1;1.2 mg/kg (maximum dose of 80 mg) at Week 2; 0.6 mg/kg (maximum dose of 40 mg) at Week 4 and Week 6.
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MSD = 0.6 mg/kg (maximum dose of 40 mg) every other week.
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FNRIEND = for MHD 0.6 mg/kg [maximum of 40 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
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FRIEND = for MHD 2.4 mg/kg [maximum of 160 mg] at the flare visit and thereafter 0.6 mg/kg (maximum dose of 40 mg) every week (until second disease flare as applicable).
2nd flare OL ADA = open-label Adalimumab 0.6 mg/kg [maximum of 40 mg] every week.
3rd flare OL ADA MAX = open-label Adalimumab 40 mg every week.
Generated: [redacted] 20[redacted]:01:48
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M11-290

本被験者は，1[redacted] 歳の男児（日本）であり，重篤な有害事象の感染性腸炎を発現した。関連する病歴は，潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎），上気道感染，慢性鼻炎及び下痢であった。

20[redacted] 年 [redacted] 月 [redacted] 日，感染性腸炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，感染性腸炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者の便の形状及び排便回数は正常であった。20[redacted] 年 [redacted] 月 [redacted] 日の朝に排便回数が増加し，便の形状は泥状となった。被験者は治験実施施設に規定外来院した。被験者によると午前中の体温は 37.6°C であったが，治験実施施設に到着時の体温は 39.0°C であった。咽頭痛，咳嗽又は鼻汁の症状はみられなかった。

発熱及び下痢の徴候及び症状が認められた。治験責任医師は，20[redacted] 年 [redacted] 月 [redacted] 日の時点で潰瘍性大腸炎の再発の可能性を否定できないと述べたが，胃腸症状の一時的な増悪は感染が原因であると判断した。外来で治療を受けながら経過観察を行うことが決定されたが，外来は休診であった。このため，20[redacted] 年 [redacted] 月 [redacted] 日に被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は解熱し，退院した。

治療薬として Fosmicin（ホスホマイシンナトリウム）が投与された。

The patient's past medications include:

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

CARBOCISTEINE for UPPER RESPIRATORYTRACT INFECTION and UPPER RESPIRATORY INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

SOLDEM 3A for PREVENTION OF DEHYDRATION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for HUMIRA (Blinded)

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1) Enteritis infectious (10058839) (Enteritis infectious (10058839)) [v.20.1] [10058839]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ENTERITIS INFECTIOUS

- Investigator: Accidental event.

- AbbVie: N/A

M10-870 主試験

治験の標題： A Multi-Center, Open-Label Study of the Human Anti-TNF Monoclonal Antibody Adalimumab to Evaluate Long-Term Safety and Tolerability of Repeated Administration of Adalimumab in Pediatric Subjects with Ulcerative Colitis Who Completed the Study M11-290	
施設数 / 実施国名： 11 施設 / ポーランド，スロバキア，英国及び米国	
治験責任医師： [redacted]., MD 他	
公表文献 (参考資料) ： 該当せず	
治験期間： 治験開始日（最初の被験者の初回来院日）：2015 年 11 月 26 日 カットオフ日：　20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ： 第 III 相
治験の種類： 第 III 相，多施設共同，非盲検試験	
目的： 本試験の目的は，M11-290 試験に参加し 52 週間の治験期間を完了した小児潰瘍性大腸炎（以下「UC」）患者に対するアダリムマブの反復投与時の長期安全性，忍容性及び臨床反応の維持効果について検討することである。	
被験者数 (計画時と解析時) ： 計画時：55 例 組入れ時：55 例 中間解析時：55 例	
診断と主要な組入れ基準： M10-870 試験の主要な選択基準は，M11-290 試験に参加し 52 週間の治験期間を完了した患者，並びに M11-290 試験中に実施した臨床評価及び臨床検査の結果に基づき，臨床状態が良好と治験責任医師が判断した患者であった。 M10-870 試験の主要な除外基準は，何らかの理由により M10-870 試験で治療を継続することが不適切と治験責任医師が判断した患者，クローン病又は分類不能大腸炎を有する患者，本試験の参加中に腸の外科切除を予定している患者，アダリムマブ又はアダリムマブの添加剤に対する過敏症の既往歴を有する患者，又は劇症腸炎若しくは中毒性巨大結腸症と診断された患者であった。	
治験方法： M10-870 試験は，小児 UC 患者におけるアダリムマブ長期投与時の臨床反応の維持効果，安全性及び忍容性を評価する第 III 相多施設共同非盲検試験である。M11-290 試験に参加し 52 週間の治験期間を完了した小児 UC 患者で，M10-870 試験の選択基準をすべて満たし，除外基準のいずれにも抵触しない患者を適格とした。すべての被験者はベースライン来院時（M11-290 試験の 52 週時来院）から非盲検下で以下の治療を受けた。 • M11-290 試験で治験薬を盲検下で投与していた被験者は，本試験のベースライン来院時からアダリムマブ 0.6 mg/kg（最大 40 mg）を非盲検下で隔週投与した。 • M11-290 試験でアダリムマブを非盲検下で投与していた被験者は，本試験でも同じ投与量を維持した。 本試験の期間は 298 週間であり，288 週間の非盲検維持療法期と，電話連絡による 70 日間の追跡調査期で構成される。 本報告は 20[redacted] 年 [redacted] 月 [redacted] 日をカットオフ日とする M10-870 試験の中間報告であり，日本以外の施設で登録され	

た被験者の結果を提示する。
被験薬，用量，投与方法及びバッチ番号： M11-290 試験で治験薬を盲検下で投与していた被験者は，本試験のベースライン来院時からアダリムマブ 0.6 mg/kg（最大 40 mg）を非盲検下で隔週投与した。M11-290 試験でアダリムマブを非盲検下で投与していた被験者は，本試験でも同じ投与量を維持した。 疾患の再燃が認められたアダリムマブ 0.6 mg/kg（最大 40 mg，体重換算）を隔週投与中の被験者は，アダリムマブ 0.6 mg/kg（最大 40 mg）を週 1 回投与できることとした。疾患の再燃が認められたアダリムマブ 0.6 mg/kg を週 1 回投与中の被験者は，アダリムマブ 40 mg（最大用量）を週 1 回投与できることとした。 アダリムマブのロット番号：[redacted]，[redacted]，[redacted]，[redacted] 治療期間：最長 288 週間
対照薬，用量，投与方法及びバッチ番号： なし
評価基準： 有効性： 本試験では主要有効性評価項目又は副次的有効性評価項目を設定しなかった。有効性評価項目は，治験期間中に部分的 Mayo スコア（以下「PMS」）により寛解（PMS が 2 ポイント以下，かつ，いずれのサブスコアも 1 ポイントを超えない）を達成した被験者の割合，治験期間中に PMS により改善（PMS が M11-290 試験のベースラインと比較して 2 ポイント以上かつ 30%以上減少）を達成した被験者の割合，治験期間中に小児潰瘍性大腸炎活動性指標（以下「PUCAI」）により寛解（10 ポイント未満）を達成した被験者の割合，治験期間中に PUCAI により改善（M11-290 試験のベースラインと比較して 20 ポイント以上の減少）を達成した被験者の割合，ベースライン時に 9 歳以上である被験者における治験期間中の IMPACT III 生活の質（以下「QOL」）総スコア及びサブスコアのベースラインからの変化，治験期間中の Work Productivity and Activity Impairment Questionnaire（以下「WPAI」）スコアのベースラインからの変化，治験期間中の身長の z スコアのベースラインからの変化，治験期間中の体格指数（以下「BMI」）のベースラインからの変化，治験期間中の年齢相応体重の z スコアのベースラインからの変化，治験期間中のアルブミン及び総たん白のベースラインからの変化，治験期間中のヘモグロビン量，ヘマトクリット値，赤血球数のベースラインからの変化，治験期間中の高感度 C 反応性たん白のベースラインからの変化，治験期間中のタナー分類で適切なステージにいる被験者の割合，治験期間中に Mayo スコア（以下「FMS」）により改善を達成した被験者の割合（FMS を得られた被験者のみ），治験期間中に FMS により寛解を達成した被験者の割合（FMS を得られた被験者のみ），治験期間中に Mayo 内視鏡所見サブスコアにより粘膜治癒（1 ポイント以下）が認められた被験者の割合（FMS を得られた被験者のみ），治験期間中に 9 ポイント FMS（医師による総合評価を除く）により寛解を達成した被験者の割合（FMS を得られた被験者のみ），並びに治験期間中に 6 ポイント FMS（医師による総合評価及び内視鏡所見サブスコアを除く）により寛解を達成した被験者の割合（FMS を得られた被験者のみ）とした。 薬物動態： 薬物動態，免疫原性及び血清学的マーカーに関する評価項目は，治験実施計画書改訂 2 版で削除した。 安全性： 治験期間中の有害事象，バイタルサインの変化，身体的所見，臨床検査値及び治験薬に係る苦情を評価した。
統計手法： 有効性： すべての解析は主試験 Full analysis set（以下「FAS」）集団を対象に実施した。主試験 FAS 集団は，M10-870 主試験で治験薬の投与を 1 回以上受けたすべての被験者とした。 薬物動態： 該当せず。 安全性： 主試験 FAS 集団について安全性の解析を行った。

要約 / 結論：

有効性：

アダリムマブを投与された被験者において，PMS 及び PUCAI により寛解及び改善を達成した被験者の割合は，投与 168 週時まで高く維持された。ただし，本試験は実施中であるため，後の評価時点ほど被験者数が少なく，結論の頑健性は低くなる。

IMPACT III 及び WPAI により評価した，アダリムマブの投与を受けた被験者の QOL 及び介護者の仕事の生産性は，ベースライン時からそれぞれ投与 120 週時及び投与 72 週時まで維持された。

薬物動態：

該当せず。

安全性：

本試験で認められたアダリムマブの安全性プロファイルは，様々な適応症で確立されているアダリムマブの安全性プロファイルと一致しており，基礎疾患から予想されるものであった。長期投与に伴う安全性プロファイルの変化は認められなかった。

アダリムマブの投与を受けた 55 例中 36 例（65.5%）に 1 件以上の有害事象が発現した。死亡又は悪性腫瘍は認められなかった。重篤な有害事象及び治験薬投与の中止に至った有害事象の発現割合は低く，認められた事象は基礎疾患から予想されるものであった。発現割合が高かった（10%以上）有害事象は，潰瘍性大腸炎及び上気道感染であった。治験薬との因果関係が関連ありと医師により判断された有害事象は 11 例に発現した。治験薬と関連ありの有害事象として関節痛が 2 例に発現し，他の事象はいずれも 1 例のみの発現であった。有害事象の大部分は重症度が軽度又は中等度であった。特に注目すべき有害事象の発現割合は低く，アダリムマブの既知の安全性プロファイルと一致しており，試験対象集団で予想されるものであった。

臨床検査（血液学的検査，血液生化学検査及び尿検査）の平均値にベースラインからの顕著な変化は認められなかった。血液学的検査値，血液生化学検査値及び尿検査値に関して，ベースラインが正常値若しくは異常高値であった検査値が最終測定時に異常低値に変動した被験者，及びベースラインが異常低値若しくは正常値であった検査値が最終測定時に異常高値に変動した被験者は少数であり，臨床的に重要ではないと判断された。

バイタルサインの平均値に，ベースラインからの顕著な変化は認められなかった。

治験期間中に妊娠は報告されなかった。

治験期間中に，治験薬又は装置に関する予期しない問題は特定されなかった。

結論：

M10-870 主試験では，アダリムマブの投与により，PMS 及び PUCAI による寛解及び改善を達成した被験者の割合は投与 168 週時まで高く維持された。

全体的にアダリムマブの安全性及び忍容性は良好であり，安全性プロファイルは過去のアダリムマブの臨床試験で確立されているものと一致していた。安全性に関する新たなリスク又は傾向は認められなかった。

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) n (%)
Any adverse event	36 (65.5)
血液およびリンパ系障害	6 (10.9)
貧血	4 (7.3)
失血性貧血	1 (1.8)
鉄欠乏性貧血	1 (1.8)
リンパ節炎	1 (1.8)
胃腸障害	21 (38.2)
腹部不快感	1 (1.8)
腹痛	1 (1.8)
上腹部痛	2 (3.6)
口唇症	1 (1.8)
潰瘍性大腸炎	11 (20.0)
便秘	1 (1.8)
下痢	1 (1.8)
消化不良	2 (3.6)
腸炎	1 (1.8)
胃炎	3 (5.5)
血便排泄	2 (3.6)
大腸ポリープ	1 (1.8)
悪心	1 (1.8)
直腸出血	1 (1.8)
嘔吐	1 (1.8)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) n (%)
一般・全身障害および投与部位の状態	2 (3.6)
末梢性浮腫	1 (1.8)
発熱	1 (1.8)
肝胆道系障害	1 (1.8)
胆嚢炎	1 (1.8)
免疫系障害	1 (1.8)
季節性アレルギー	1 (1.8)
感染症および寄生虫症	20 (36.4)
肛門膿瘍	1 (1.8)
気管支炎	3 (5.5)
ウイルス性胃腸炎	2 (3.6)
帯状疱疹	1 (1.8)
上咽頭炎	3 (5.5)
口腔ヘルペス	1 (1.8)
中耳炎	1 (1.8)
咽頭炎	2 (3.6)
副鼻腔炎	1 (1.8)
歯膿瘍	1 (1.8)
上気道感染	6 (10.9)
尿路感染	2 (3.6)
ウイルス感染	2 (3.6)
ウイルス性上気道感染	2 (3.6)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) n (%)
感染症および寄生虫症 (Cont.)	
外陰膣炎	1 (1.8)
傷害、中毒および処置合併症	5 (9.1)
足関節部骨折	1 (1.8)
手骨折	1 (1.8)
四肢損傷	1 (1.8)
上肢骨折	1 (1.8)
手首関節骨折	1 (1.8)
臨床検査	6 (10.9)
血中アルカリホスファターゼ増加	1 (1.8)
体温上昇	1 (1.8)
結核菌群検査陽性	4 (7.3)
筋骨格系および結合組織障害	7 (12.7)
関節痛	4 (7.3)
背部痛	1 (1.8)
成長不全	1 (1.8)
若年性特発性関節炎	1 (1.8)
脊椎痛	1 (1.8)
神経系障害	6 (10.9)
頭痛	5 (9.1)
傾眠	1 (1.8)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) n (%)
精神障害	2 (3.6)
うつ病	2 (3.6)
腎および尿路障害	3 (5.5)
血尿	1 (1.8)
腎結石症	1 (1.8)
腎仙痛	1 (1.8)
生殖系および乳房障害	3 (5.5)
月経困難症	1 (1.8)
卵巣嚢胞	2 (3.6)
呼吸器、胸郭および縦隔障害	4 (7.3)
喘息	1 (1.8)
鼻出血	1 (1.8)
アレルギー性鼻炎	2 (3.6)
鼻漏	1 (1.8)
皮膚および皮下組織障害	4 (7.3)
乾癬様皮膚炎	1 (1.8)
乾癬	1 (1.8)
発疹	1 (1.8)
皮膚障害	1 (1.8)
血管障害	1 (1.8)
高血圧	1 (1.8)

表 1.　　すべての有害事象（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）（続き）

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

相互参照：M10-870 主試験 中間 CSR Table 14.3__1.2.1.1

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
Any adverse event	36 (65.5)
No Reasonable Possibility	25 (45.5)
Reasonable Possibility	11 (20.0)
血液およびリンパ系障害	6 (10.9)
No Reasonable Possibility	6 (10.9)
貧血	4 (7.3)
No Reasonable Possibility	4 (7.3)
失血性貧血	1 (1.8)
No Reasonable Possibility	1 (1.8)
鉄欠乏性貧血	1 (1.8)
No Reasonable Possibility	1 (1.8)
リンパ節炎	1 (1.8)
No Reasonable Possibility	1 (1.8)
胃腸障害	21 (38.2)
No Reasonable Possibility	19 (34.5)
Reasonable Possibility	2 (3.6)
腹部不快感	1 (1.8)
No Reasonable Possibility	1 (1.8)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
胃腸障害 (Cont.)	
腹痛	1 (1.8)
No Reasonable Possibility	1 (1.8)
上腹部痛	2 (3.6)
No Reasonable Possibility	2 (3.6)
口唇症	1 (1.8)
No Reasonable Possibility	1 (1.8)
潰瘍性大腸炎	11 (20.0)
No Reasonable Possibility	10 (18.2)
Reasonable Possibility	1 (1.8)
便秘	1 (1.8)
No Reasonable Possibility	1 (1.8)
下痢	1 (1.8)
No Reasonable Possibility	1 (1.8)
消化不良	2 (3.6)
No Reasonable Possibility	2 (3.6)
腸炎	1 (1.8)
No Reasonable Possibility	1 (1.8)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
胃腸障害 (Cont.)	
胃炎	3 (5.5)
No Reasonable Possibility	2 (3.6)
Reasonable Possibility	1 (1.8)
血便排泄	2 (3.6)
No Reasonable Possibility	2 (3.6)
大腸ポリープ	1 (1.8)
No Reasonable Possibility	1 (1.8)
悪心	1 (1.8)
No Reasonable Possibility	1 (1.8)
直腸出血	1 (1.8)
No Reasonable Possibility	1 (1.8)
嘔吐	1 (1.8)
No Reasonable Possibility	1 (1.8)
一般・全身障害および投与部位の状態	2 (3.6)
No Reasonable Possibility	1 (1.8)
Reasonable Possibility	1 (1.8)
末梢性浮腫	1 (1.8)
No Reasonable Possibility	1 (1.8)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
一般・全身障害および投与部位の状態 (Cont.)	
発熱	1 (1.8)
Reasonable Possibility	1 (1.8)
肝胆道系障害	1 (1.8)
Reasonable Possibility	1 (1.8)
胆嚢炎	1 (1.8)
Reasonable Possibility	1 (1.8)
免疫系障害	1 (1.8)
No Reasonable Possibility	1 (1.8)
季節性アレルギー	1 (1.8)
No Reasonable Possibility	1 (1.8)
感染症および寄生虫症	20 (36.4)
No Reasonable Possibility	17 (30.9)
Reasonable Possibility	3 (5.5)
肛門膿瘍	1 (1.8)
Reasonable Possibility	1 (1.8)
気管支炎	3 (5.5)
No Reasonable Possibility	3 (5.5)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
感染症および寄生虫症 (Cont.)	
ウイルス性胃腸炎	2 (3.6)
No Reasonable Possibility	2 (3.6)
帯状疱疹	1 (1.8)
Reasonable Possibility	1 (1.8)
上咽頭炎	3 (5.5)
No Reasonable Possibility	3 (5.5)
口腔ヘルペス	1 (1.8)
No Reasonable Possibility	1 (1.8)
中耳炎	1 (1.8)
No Reasonable Possibility	1 (1.8)
咽頭炎	2 (3.6)
No Reasonable Possibility	2 (3.6)
副鼻腔炎	1 (1.8)
No Reasonable Possibility	1 (1.8)
歯膿瘍	1 (1.8)
No Reasonable Possibility	1 (1.8)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
感染症および寄生虫症 (Cont.)	
上気道感染	6 (10.9)
No Reasonable Possibility	5 (9.1)
Reasonable Possibility	1 (1.8)
尿路感染	2 (3.6)
No Reasonable Possibility	2 (3.6)
ウイルス感染	2 (3.6)
No Reasonable Possibility	2 (3.6)
ウイルス性上気道感染	2 (3.6)
No Reasonable Possibility	2 (3.6)
外陰膣炎	1 (1.8)
No Reasonable Possibility	1 (1.8)
傷害、中毒および処置合併症	5 (9.1)
No Reasonable Possibility	5 (9.1)
足関節部骨折	1 (1.8)
No Reasonable Possibility	1 (1.8)
手骨折	1 (1.8)
No Reasonable Possibility	1 (1.8)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
傷害、中毒および処置合併症 (Cont.)	
四肢損傷	1 (1.8)
No Reasonable Possibility	1 (1.8)
上肢骨折	1 (1.8)
No Reasonable Possibility	1 (1.8)
手首関節骨折	1 (1.8)
No Reasonable Possibility	1 (1.8)
臨床検査	6 (10.9)
No Reasonable Possibility	5 (9.1)
Reasonable Possibility	1 (1.8)
血中アルカリホスファターゼ増加	1 (1.8)
No Reasonable Possibility	1 (1.8)
体温上昇	1 (1.8)
No Reasonable Possibility	1 (1.8)
結核菌群検査陽性	4 (7.3)
No Reasonable Possibility	3 (5.5)
Reasonable Possibility	1 (1.8)
筋骨格系および結合組織障害	7 (12.7)
No Reasonable Possibility	5 (9.1)
Reasonable Possibility	2 (3.6)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
筋骨格系および結合組織障害 (Cont.)	
関節痛	4 (7.3)
No Reasonable Possibility	2 (3.6)
Reasonable Possibility	2 (3.6)
背部痛	1 (1.8)
No Reasonable Possibility	1 (1.8)
成長不全	1 (1.8)
No Reasonable Possibility	1 (1.8)
若年性特発性関節炎	1 (1.8)
No Reasonable Possibility	1 (1.8)
脊椎痛	1 (1.8)
No Reasonable Possibility	1 (1.8)
神経系障害	6 (10.9)
No Reasonable Possibility	6 (10.9)
頭痛	5 (9.1)
No Reasonable Possibility	5 (9.1)
傾眠	1 (1.8)
No Reasonable Possibility	1 (1.8)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
精神障害	2 (3.6)
No Reasonable Possibility	2 (3.6)
うつ病	2 (3.6)
No Reasonable Possibility	2 (3.6)
腎および尿路障害	3 (5.5)
No Reasonable Possibility	2 (3.6)
Reasonable Possibility	1 (1.8)
血尿	1 (1.8)
No Reasonable Possibility	1 (1.8)
腎結石症	1 (1.8)
Reasonable Possibility	1 (1.8)
腎仙痛	1 (1.8)
No Reasonable Possibility	1 (1.8)
生殖系および乳房障害	3 (5.5)
No Reasonable Possibility	2 (3.6)
Reasonable Possibility	1 (1.8)
月経困難症	1 (1.8)
No Reasonable Possibility	1 (1.8)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
生殖系および乳房障害 (Cont.)	
卵巣嚢胞	2 (3.6)
No Reasonable Possibility	1 (1.8)
Reasonable Possibility	1 (1.8)
呼吸器、胸郭および縦隔障害	4 (7.3)
No Reasonable Possibility	4 (7.3)
喘息	1 (1.8)
No Reasonable Possibility	1 (1.8)
鼻出血	1 (1.8)
No Reasonable Possibility	1 (1.8)
アレルギー性鼻炎	2 (3.6)
No Reasonable Possibility	2 (3.6)
鼻漏	1 (1.8)
No Reasonable Possibility	1 (1.8)
皮膚および皮下組織障害	4 (7.3)
No Reasonable Possibility	1 (1.8)
Reasonable Possibility	3 (5.5)
乾癬様皮膚炎	1 (1.8)
Reasonable Possibility	1 (1.8)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=55) n (%)
皮膚および皮下組織障害 (Cont.)	
乾癬	1 (1.8)
Reasonable Possibility	1 (1.8)
発疹	1 (1.8)
No Reasonable Possibility	1 (1.8)
皮膚障害	1 (1.8)
Reasonable Possibility	1 (1.8)
血管障害	1 (1.8)
No Reasonable Possibility	1 (1.8)
高血圧	1 (1.8)
No Reasonable Possibility	1 (1.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown", unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

相互参照：M10-870 主試験 中間 CSR Table 14.3__1.3.1

M10-870 日本サブ試験

治験の標題： A Multi-Center, Open-Label Study of the Human Anti-TNF Monoclonal Antibody Adalimumab to Evaluate Long-Term Safety and Tolerability of Repeated Administration of Adalimumab in Pediatric Subjects with Ulcerative Colitis Who Completed the Study M11-290	
施設数 / 実施国名： 主試験：11 施設 / ポーランド，スロバキア，英国及び米国 日本サブ試験：3 施設 / 日本	
治験責任医師： [redacted] MD 他	
公表文献 (参考資料) ： 該当せず	
治験期間： 治験開始日（最初の被験者の初回来院日）： 主試験： 2015 年 11 月 26 日 日本サブ試験： 20[redacted] 年 [redacted] 月 [redacted] 日 カットオフ日： 20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ： 第 III 相
治験の種類： 第 III 相，多施設共同，非盲検試験	
目的： 本試験の目的は，M11-290 試験に参加し 52 週間の治験期間を完了した小児潰瘍性大腸炎（以下「UC」）患者に対するアダリムマブの反復投与時の長期安全性，忍容性及び臨床反応の維持効果について検討することである。	
被験者数 (計画時と解析時) ： 計画時：約 60 例（主試験 55 例，日本サブ試験 5 例） 組入れ時：59 例（主試験 55 例，日本サブ試験 4 例） 中間解析時：59 例（主試験 55 例，日本サブ試験 4 例）	
診断と主要な組入れ基準： M11-290 試験に参加し 52 週間の治験期間を完了した，年齢が 4～17 歳の中等症から重症の小児 UC 患者で，本試験の選択基準をすべて満たし，除外基準のいずれにも抵触しない患者を適格とした。	
治験方法： M10-870 試験は，小児 UC 患者におけるアダリムマブ長期投与時の臨床反応の維持効果，安全性及び忍容性を評価する第 III 相多施設共同非盲検試験である。本試験は，日本以外の施設で登録された被験者を対象とする主試験と，日本の施設で登録された被験者を対象とする日本サブ試験で構成される。M10-870 日本サブ試験は，科学的な目的及び規制要件に適合するため，M11-290 日本サブ試験に約 8 例の被験者を組み入れる計画であり，M10-870 日本サブ試験ではそのうちの約 5 例の参加を予定し，倫理的な観点から不必要に多くの被験者を組み入れないこととした。すべての被験者はベースライン来院時（M11-290 試験の 52 週時来院）から非盲検下で治療を受けた。 本報告では，20[redacted] 年 [redacted] 月 [redacted] 日をカットオフ日とする M10-870 日本サブ試験の中間報告として，日本の施設で登録された被験者の結果を，日本以外の施設で登録された被験者（M10-870 主試験）の結果と統合して提示する。	

被験薬，用量，投与方法及びバッチ番号：

M11-290 試験で治験薬を盲検下で投与していた被験者は，本試験のベースライン来院時からアダリムマブ 0.6 mg/kg（最大 40 mg）を非盲検下で隔週投与した。M11-290 試験でアダリムマブを非盲検下で投与していた被験者は，本試験でも同じ投与量を維持した。

疾患の再燃が認められたアダリムマブ 0.6 mg/kg（最大 40 mg，体重換算）を隔週投与中の被験者は，アダリムマブ 0.6 mg/kg（最大 40 mg）を週 1 回投与できることとした。疾患の再燃が認められたアダリムマブ 0.6 mg/kg を週 1 回投与中の被験者は，アダリムマブ 40 mg（最大用量）を週 1 回投与できることとした。

アダリムマブのロット番号：[redacted]

治療期間：最長 288 週間

対照薬，用量，投与方法及びバッチ番号：

なし

評価基準：

有効性：

本試験では主要有効性評価項目又は副次的有効性評価項目を設定しなかった。有効性評価項目は，治験期間中に部分的 Mayo スコア（以下「PMS」）により寛解（PMS が 2 ポイント以下，かつ，いずれのサブスコアも 1 ポイントを超えない）を達成した被験者の割合，治験期間中に PMS により改善（PMS が M11-290 試験のベースラインと比較して 2 ポイント以上かつ 30%以上減少）を達成した被験者の割合，治験期間中に小児潰瘍性大腸炎活動性指標（以下「PUCAI」）により寛解（10 ポイント未満）を達成した被験者の割合，治験期間中に PUCAI により改善（M11-290 試験のベースラインと比較して 20 ポイント以上の減少）を達成した被験者の割合，ベースライン時に 9 歳以上である被験者における治験期間中の IMPACT III 生活の質（以下「QOL」）総スコア及びサブスコアのベースラインからの変化，治験期間中の Work Productivity and Activity Impairment Questionnaire（以下「WPAI」）スコアのベースラインからの変化，治験期間中の身長の z スコアのベースラインからの変化，治験期間中の体格指数（以下「BMI」）のベースラインからの変化，治験期間中の年齢相応体重の z スコアのベースラインからの変化，治験期間中のアルブミン及び総たん白のベースラインからの変化，治験期間中のヘモグロビン量，ヘマトクリット値，赤血球数のベースラインからの変化，治験期間中の高感度 C 反応性たん白のベースラインからの変化，治験期間中のタナー分類で適切なステージにいる被験者の割合，治験期間中に Mayo スコア（以下「FMS」）により改善を達成した被験者の割合（FMS を得られた被験者のみ），治験期間中に FMS により寛解を達成した被験者の割合（FMS を得られた被験者のみ），治験期間中に Mayo 内視鏡所見サブスコアにより粘膜治癒（1 ポイント以下）が認められた被験者の割合（FMS を得られた被験者のみ），治験期間中に 9 ポイント FMS（医師による総合評価を除く）により寛解を達成した被験者の割合（FMS を得られた被験者のみ），並びに治験期間中に 6 ポイント FMS（医師による総合評価及び内視鏡所見サブスコアを除く）により寛解を達成した被験者の割合（FMS を得られた被験者のみ）とした。

薬物動態：

薬物動態，免疫原性及び血清学的マーカーに関する評価項目は，治験実施計画書改訂 2 版で削除した。

安全性：

治験期間中の有害事象，バイタルサインの変化，身体的所見，臨床検査値及び治験薬に係る苦情を評価した。

統計手法：

有効性：

すべての解析は統合 Full analysis set（以下「FAS」）集団を対象に実施した。統合 FAS 集団は，M10-870 日本サブ試験で治験薬の投与を 1 回以上受けたすべての日本の被験者，及び M10-870 主試験で治験薬の投与を 1 回以上受けたすべての日本以外の被験者の計 59 例とした。

薬物動態：

該当せず。

安全性：

統合 FAS 集団について安全性の解析を行った。なお，日本の被験者数は少ないため（統合 FAS 集団 59 例，う

ち日本人被験者は 4 例），安全性の解析には統合集団を使用した。
要約 / 結論： 有効性： アダリムマブを投与された被験者において，PMS 及び PUCAI により寛解及び改善を達成した被験者の割合は，投与 144 週時まで高く維持された。ただし，本試験は実施中であるため，後の評価時点ほど被験者数が少なく，結論の頑健性は低くなる。 IMPACT III 及び WPAI により評価した，アダリムマブの投与を受けた被験者の QOL 及び介護者の仕事の生産性は，ベースライン時からそれぞれ投与 96 週時及び投与 120 週時まで維持された。
薬物動態： 該当せず。
安全性： 本試験で認められたアダリムマブの安全性プロファイルは，様々な適応症で確立されているアダリムマブの安全性プロファイルと一致しており，基礎疾患から予想されるものであった。長期投与に伴う安全性プロファイルの変化は認められなかった。 アダリムマブの投与を受けた 59 例中 40 例（67.8%）に 1 件以上の有害事象が発現した。死亡又は悪性腫瘍は認められなかった。重篤な有害事象及び治験薬投与の中止に至った有害事象の発現割合は低く，認められた事象は基礎疾患から予想されるものであった。発現割合が高かった（10%以上）有害事象は，潰瘍性大腸炎及び上気道感染であった。有害事象の大部分は重症度が軽度又は中等度であった。特に注目すべき有害事象の発現割合は低く，アダリムマブの既知の安全性プロファイルと一致しており，試験対象集団で予想されるものであった。 臨床検査（血液学的検査，血液生化学検査及び尿検査）の平均値にベースラインからの顕著な変化は認められなかった。血液学的検査値，血液生化学検査値及び尿検査値に関して，ベースラインが正常値若しくは異常高値であった検査値が最終測定時に異常低値に変動した被験者，及びベースラインが異常低値若しくは正常値であった検査値が最終測定時に異常高値に変動した被験者は少数であり，臨床的に重要ではないと判断された。 バイタルサインの平均値に，ベースラインからの顕著な変化は認められなかった。 治験期間中に妊娠は報告されなかった。 治験期間中に，治験薬又は装置に関する予期しない問題は特定されなかった。
結論： M10-870 主試験及び M10-870 日本サブ試験を統合解析した結果，アダリムマブの投与により，寛解及び改善を達成した被験者の割合は投与 144 週時まで高く維持された。 全体的にアダリムマブの安全性及び忍容性は良好であり，安全性プロファイルは過去のアダリムマブの臨床試験で確立されているものと一致していた。安全性に関する新たなリスク又は傾向は認められなかった。M10-870 主試験と M10-870 日本サブ試験の結果は一貫しており，日本の中等症から重症の小児 UC 患者におけるアダリムマブの有効性及び安全性が裏付けられた。

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合 FAS 集団，M10-870 試験）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=59) n (%)
Any adverse event	40 (67.8)
血液およびリンパ系障害	6 (10.2)
貧血	4 (6.8)
失血性貧血	1 (1.7)
鉄欠乏性貧血	1 (1.7)
リンパ節炎	1 (1.7)
眼障害	1 (1.7)
近視	1 (1.7)
胃腸障害	23 (39.0)
腹部不快感	1 (1.7)
腹痛	1 (1.7)
上腹部痛	2 (3.4)
口唇症	1 (1.7)
潰瘍性大腸炎	12 (20.3)
便秘	1 (1.7)
下痢	1 (1.7)
消化不良	2 (3.4)
腸炎	1 (1.7)
胃炎	3 (5.1)
血便排泄	2 (3.4)
大腸ポリープ	1 (1.7)
悪心	2 (3.4)
直腸出血	1 (1.7)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=59) n (%)
胃腸障害 (Cont.)	
口内炎	1 (1.7)
嘔吐	1 (1.7)
一般・全身障害および投与部位の状態	4 (6.8)
倦怠感	1 (1.7)
末梢性浮腫	1 (1.7)
発熱	2 (3.4)
肝胆道系障害	1 (1.7)
胆嚢炎	1 (1.7)
免疫系障害	1 (1.7)
季節性アレルギー	1 (1.7)
感染症および寄生虫症	24 (40.7)
肛門膿瘍	1 (1.7)
気管支炎	3 (5.1)
ウイルス性胃腸炎	2 (3.4)
帯状疱疹	2 (3.4)
膿痂疹	1 (1.7)
上咽頭炎	5 (8.5)
口腔ヘルペス	1 (1.7)
中耳炎	1 (1.7)
咽頭炎	4 (6.8)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=59) n (%)
感染症および寄生虫症 (Cont.)	
敗血症	1 (1.7)
副鼻腔炎	1 (1.7)
レンサ球菌感染	1 (1.7)
歯膿瘍	1 (1.7)
上気道感染	7 (11.9)
尿路感染	2 (3.4)
ウイルス感染	2 (3.4)
ウイルス性上気道感染	2 (3.4)
外陰腟炎	1 (1.7)
傷害、中毒および処置合併症	5 (8.5)
足関節部骨折	1 (1.7)
手骨折	1 (1.7)
四肢損傷	1 (1.7)
上肢骨折	1 (1.7)
手首関節骨折	1 (1.7)
臨床検査	6 (10.2)
血中アルカリホスファターゼ増加	1 (1.7)
体温上昇	1 (1.7)
結核菌群検査陽性	4 (6.8)
代謝および栄養障害	1 (1.7)
食欲減退	1 (1.7)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=59) n (%)
筋骨格系および結合組織障害	7 (11.9)
関節痛	4 (6.8)
背部痛	1 (1.7)
成長不全	1 (1.7)
若年性特発性関節炎	1 (1.7)
脊椎痛	1 (1.7)
神経系障害	6 (10.2)
頭痛	5 (8.5)
傾眠	1 (1.7)
精神障害	2 (3.4)
うつ病	2 (3.4)
腎および尿路障害	3 (5.1)
血尿	1 (1.7)
腎結石症	1 (1.7)
腎仙痛	1 (1.7)
生殖系および乳房障害	3 (5.1)
月経困難症	1 (1.7)
卵巣嚢胞	2 (3.4)
呼吸器、胸郭および縦隔障害	4 (6.8)
喘息	1 (1.7)
鼻出血	1 (1.7)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=59) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)	
アレルギー性鼻炎	2 (3.4)
鼻漏	1 (1.7)
皮膚および皮下組織障害	5 (8.5)
皮膚炎	1 (1.7)
乾癬様皮膚炎	1 (1.7)
乾癬	1 (1.7)
発疹	1 (1.7)
皮膚障害	1 (1.7)
蕁麻疹	1 (1.7)
血管障害	1 (1.7)
高血圧	1 (1.7)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

相互参照：M10-870 日本サブ試験 中間 CSR Table 14.3__1.2.1.1_A

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
Any adverse event	40 (67.8)
No Reasonable Possibility	27 (45.8)
Reasonable Possibility	13 (22.0)
血液およびリンパ系障害	6 (10.2)
No Reasonable Possibility	6 (10.2)
貧血	4 (6.8)
No Reasonable Possibility	4 (6.8)
失血性貧血	1 (1.7)
No Reasonable Possibility	1 (1.7)
鉄欠乏性貧血	1 (1.7)
No Reasonable Possibility	1 (1.7)
リンパ節炎	1 (1.7)
No Reasonable Possibility	1 (1.7)
眼障害	1 (1.7)
No Reasonable Possibility	1 (1.7)
近視	1 (1.7)
No Reasonable Possibility	1 (1.7)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
胃腸障害	23 (39.0)
No Reasonable Possibility	21 (35.6)
Reasonable Possibility	2 (3.4)
腹部不快感	1 (1.7)
No Reasonable Possibility	1 (1.7)
腹痛	1 (1.7)
No Reasonable Possibility	1 (1.7)
上腹部痛	2 (3.4)
No Reasonable Possibility	2 (3.4)
口唇症	1 (1.7)
No Reasonable Possibility	1 (1.7)
潰瘍性大腸炎	12 (20.3)
No Reasonable Possibility	11 (18.6)
Reasonable Possibility	1 (1.7)
便秘	1 (1.7)
No Reasonable Possibility	1 (1.7)
下痢	1 (1.7)
No Reasonable Possibility	1 (1.7)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
胃腸障害 (Cont.)	
消化不良	2 (3.4)
No Reasonable Possibility	2 (3.4)
腸炎	1 (1.7)
No Reasonable Possibility	1 (1.7)
胃炎	3 (5.1)
No Reasonable Possibility	2 (3.4)
Reasonable Possibility	1 (1.7)
血便排泄	2 (3.4)
No Reasonable Possibility	2 (3.4)
大腸ポリープ	1 (1.7)
No Reasonable Possibility	1 (1.7)
悪心	2 (3.4)
No Reasonable Possibility	2 (3.4)
直腸出血	1 (1.7)
No Reasonable Possibility	1 (1.7)
口内炎	1 (1.7)
No Reasonable Possibility	1 (1.7)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
胃腸障害 (Cont.)	
嘔吐	1 (1.7)
No Reasonable Possibility	1 (1.7)
一般・全身障害および投与部位の状態	4 (6.8)
No Reasonable Possibility	3 (5.1)
Reasonable Possibility	1 (1.7)
倦怠感	1 (1.7)
No Reasonable Possibility	1 (1.7)
末梢性浮腫	1 (1.7)
No Reasonable Possibility	1 (1.7)
発熱	2 (3.4)
No Reasonable Possibility	1 (1.7)
Reasonable Possibility	1 (1.7)
肝胆道系障害	1 (1.7)
Reasonable Possibility	1 (1.7)
胆嚢炎	1 (1.7)
Reasonable Possibility	1 (1.7)
免疫系障害	1 (1.7)
No Reasonable Possibility	1 (1.7)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
免疫系障害 (Cont.)	
季節性アレルギー	1 (1.7)
No Reasonable Possibility	1 (1.7)
感染症および寄生虫症	24 (40.7)
No Reasonable Possibility	19 (32.2)
Reasonable Possibility	5 (8.5)
肛門膿瘍	1 (1.7)
Reasonable Possibility	1 (1.7)
気管支炎	3 (5.1)
No Reasonable Possibility	3 (5.1)
ウイルス性胃腸炎	2 (3.4)
No Reasonable Possibility	2 (3.4)
帯状疱疹	2 (3.4)
Reasonable Possibility	2 (3.4)
膿痂疹	1 (1.7)
No Reasonable Possibility	1 (1.7)
上咽頭炎	5 (8.5)
No Reasonable Possibility	5 (8.5)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
感染症および寄生虫症 (Cont.)	
口腔ヘルペス	1 (1.7)
No Reasonable Possibility	1 (1.7)
中耳炎	1 (1.7)
No Reasonable Possibility	1 (1.7)
咽頭炎	4 (6.8)
No Reasonable Possibility	4 (6.8)
敗血症	1 (1.7)
No Reasonable Possibility	1 (1.7)
副鼻腔炎	1 (1.7)
No Reasonable Possibility	1 (1.7)
レンサ球菌感染	1 (1.7)
No Reasonable Possibility	1 (1.7)
歯膿瘍	1 (1.7)
No Reasonable Possibility	1 (1.7)
上気道感染	7 (11.9)
No Reasonable Possibility	5 (8.5)
Reasonable Possibility	2 (3.4)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
感染症および寄生虫症 (Cont.)	
尿路感染	2 (3.4)
No Reasonable Possibility	2 (3.4)
ウイルス感染	2 (3.4)
No Reasonable Possibility	2 (3.4)
ウイルス性上気道感染	2 (3.4)
No Reasonable Possibility	2 (3.4)
外陰膣炎	1 (1.7)
No Reasonable Possibility	1 (1.7)
傷害、中毒および処置合併症	5 (8.5)
No Reasonable Possibility	5 (8.5)
足関節部骨折	1 (1.7)
No Reasonable Possibility	1 (1.7)
手骨折	1 (1.7)
No Reasonable Possibility	1 (1.7)
四肢損傷	1 (1.7)
No Reasonable Possibility	1 (1.7)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
傷害、中毒および処置合併症 (Cont.)	
上肢骨折	1 (1.7)
No Reasonable Possibility	1 (1.7)
手首関節骨折	1 (1.7)
No Reasonable Possibility	1 (1.7)
臨床検査	6 (10.2)
No Reasonable Possibility	5 (8.5)
Reasonable Possibility	1 (1.7)
血中アルカリホスファターゼ増加	1 (1.7)
No Reasonable Possibility	1 (1.7)
体温上昇	1 (1.7)
No Reasonable Possibility	1 (1.7)
結核菌群検査陽性	4 (6.8)
No Reasonable Possibility	3 (5.1)
Reasonable Possibility	1 (1.7)
代謝および栄養障害	1 (1.7)
No Reasonable Possibility	1 (1.7)
食欲減退	1 (1.7)
No Reasonable Possibility	1 (1.7)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
筋骨格系および結合組織障害	7 (11.9)
No Reasonable Possibility	5 (8.5)
Reasonable Possibility	2 (3.4)
関節痛	4 (6.8)
No Reasonable Possibility	2 (3.4)
Reasonable Possibility	2 (3.4)
背部痛	1 (1.7)
No Reasonable Possibility	1 (1.7)
成長不全	1 (1.7)
No Reasonable Possibility	1 (1.7)
若年性特発性関節炎	1 (1.7)
No Reasonable Possibility	1 (1.7)
脊椎痛	1 (1.7)
No Reasonable Possibility	1 (1.7)
神経系障害	6 (10.2)
No Reasonable Possibility	6 (10.2)
頭痛	5 (8.5)
No Reasonable Possibility	5 (8.5)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
神経系障害 (Cont.)	
傾眠	1 (1.7)
No Reasonable Possibility	1 (1.7)
精神障害	2 (3.4)
No Reasonable Possibility	2 (3.4)
うつ病	2 (3.4)
No Reasonable Possibility	2 (3.4)
腎および尿路障害	3 (5.1)
No Reasonable Possibility	2 (3.4)
Reasonable Possibility	1 (1.7)
血尿	1 (1.7)
No Reasonable Possibility	1 (1.7)
腎結石症	1 (1.7)
Reasonable Possibility	1 (1.7)
腎仙痛	1 (1.7)
No Reasonable Possibility	1 (1.7)
生殖系および乳房障害	3 (5.1)
No Reasonable Possibility	2 (3.4)
Reasonable Possibility	1 (1.7)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
生殖系および乳房障害 (Cont.)	
月経困難症	1 (1.7)
No Reasonable Possibility	1 (1.7)
卵巣嚢胞	2 (3.4)
No Reasonable Possibility	1 (1.7)
Reasonable Possibility	1 (1.7)
呼吸器、胸郭および縦隔障害	4 (6.8)
No Reasonable Possibility	4 (6.8)
喘息	1 (1.7)
No Reasonable Possibility	1 (1.7)
鼻出血	1 (1.7)
No Reasonable Possibility	1 (1.7)
アレルギー性鼻炎	2 (3.4)
No Reasonable Possibility	2 (3.4)
鼻漏	1 (1.7)
No Reasonable Possibility	1 (1.7)
皮膚および皮下組織障害	5 (8.5)
No Reasonable Possibility	2 (3.4)
Reasonable Possibility	3 (5.1)

表 2. すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	Adalimumab (N=59) n (%)
皮膚および皮下組織障害 (Cont.)	
皮膚炎	1 (1.7)
No Reasonable Possibility	1 (1.7)
乾癬様皮膚炎	1 (1.7)
Reasonable Possibility	1 (1.7)
乾癬	1 (1.7)
Reasonable Possibility	1 (1.7)
発疹	1 (1.7)
No Reasonable Possibility	1 (1.7)
皮膚障害	1 (1.7)
Reasonable Possibility	1 (1.7)
蕁麻疹	1 (1.7)
No Reasonable Possibility	1 (1.7)
血管障害	1 (1.7)
No Reasonable Possibility	1 (1.7)
高血圧	1 (1.7)
No Reasonable Possibility	1 (1.7)

表 2.　　すべての有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合 FAS 集団，M10-870 試験）（続き）

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

相互参照：M10-870 日本サブ試験 中間 CSR Table 14.3__1.3.1_A

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
気管支炎	X			
喘息	X			
成長不全	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EW	[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: ANAEMIA DUE TO ULCERATIVE COLITIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: SINCE 20[redacted]	20[redacted]
MURMUR: FUNCTIONAL MURMUR WITHOUT CHANGES IN ECHOCARDIOGRAPHY	20[redacted]
OTHER: UNDERWEIGHT	20[redacted]
TRANSFUSIONS: PATIENT REQUIRED TRANSFUSION DUE TO ANAEMIA IN DECURSU ULCERATIVE COLITIS	20[redacted]
Ulcerative colitis	20[redacted]
PANCREATITIS: TWICE 1. IDIOPATHIC 2. DUE TO IMMUNOSUPPRESSANT USE	20[redacted]
OTHER: GROWTH FAILURE	20[redacted]
SKIN DISORDERS: HIRSUTISM	20[redacted]
HYPERTENSION: DIAGNOSED AND TREATED DUE TO HYPERTENSION	20[redacted]
MIGRAINE HEADACHE: HEADACHE PROPABLY DUE TO HYPERTENSION	20[redacted]
SURGERY: WOUND OF LEFT UPPER LEG(SUTURED)	20[redacted]
OTHER: NYCTURIA	20[redacted]

Prior Procedures	Procedure Year
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD-MHD-FREIND				[redacted]20[redacted] / 1	[redacted]20[redacted] / 358	371
Adalimumab	0.8 ML	SUBCUTANEOUSLY	EW	[redacted]20[redacted] / 373	[redacted]20[redacted] / 959	600

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
CROMOGLICATE SODIUM	1 CAPS	TID	Y-M: 20[redacted]-[redacted]
AZATHIOPRINE	25 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted]
COLECALCIFEROL	500 IU (international unit(s))	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	100 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted]
BISOPROLOL FUMARATE	1.25 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -199
POTASSIUM	5 mL (millilitre(s))	BID	Y-M: 20[redacted]-[redacted] / -118
VANCOMYCIN	250 mg (milligram(s))	QID	Y-M: 20[redacted]-[redacted] / -36
CIPROFLOXACIN	250 mg (milligram(s))	BID	Y-M: 20[redacted]-[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
COLECALCIFEROL	500 IU (international unit(s))	QD	Y-M: 20[redacted]-[redacted]	Y-M: 20[redacted]-[redacted] / 525
BISOPROLOL FUMARATE	1.25 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / - 199	ONGOING
POTASSIUM	5 mL (millilitre(s))	BID	Y-M: 20[redacted]-[redacted] / - 118	ONGOING
SACCHAROMYCES BOULARDII	250 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 193	Y-M: 20[redacted]-[redacted] / 540
ISONIAZID	100 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 405	Y-M: 20[redacted]-[redacted] / 588
VITAMINUM	1 TABLET	QD	Y-M: 20[redacted]-[redacted] / 405	Y-M: 20[redacted]-[redacted] / 588
METHYLPREDNISOLONE	2 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 457	Y-M: 20[redacted]-[redacted] / 511

METHYLPREDNISOLONE	8 mg (milligram(s))	QD	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 550
COLECALCIFEROL	1000 IU/kg (IU/kilogram)	QD	Y-M: 20[redacted] / 526	ONGOING
CIPROFLOXACIN	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 526	Y-M: 20[redacted] / 540
FLUCONAZOLE	15 mL (millilitre(s))	QD	Y-M: 20[redacted] / 526	Y-M: 20[redacted] / 540
METHYLPREDNISOLONE	6 mg (milligram(s))	QD	Y-M: 20[redacted] / 551	Y-M: 20[redacted] / 624
METHYLPREDNISOLONE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / 625	Y-M: 20[redacted] / 965
SOMATROPIN	0.45 mg (milligram(s))	OTHER: 5 X (FROM MONDAY TO FRIDAY)	Y-M: 20[redacted] / 953	ONGOING
SOMATROPIN	0.5 mg/kg (milligram(s)/kilogram)	OTHER: 2 X (SAT AND SUNDAY)	Y-M: 20[redacted] / 953	ONGOING
METHYLPREDNISOLONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 966	ONGOING

Event #1: Serious Adverse Event

Event Description	BRONCHITIS
Preferred term	気管支炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 524
Age at AE Onset	[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx DAY 496): ADENOVIRUS: NEGATIVE [0 - 0] UNIT NOT REPORTED; [redacted]20[redacted] (Rx DAY 525): AMYLASE: 42.47 [0 - 0] U/L; CLOSTRIDIUM DIFFICII: NEGATIVE [0 - 0] UNIT NOT REPORTED; D3 VITAMIN: 24.21 [20 - 60] NG/ML; IRON: 20.49 [0 - 0] UG/DL; LEUCOCYTES: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; SEDIMENTARION RATIO: 34 [0 - 0] MM/HR; UREA: 22.85 [0 - 0] MG/DL; [redacted]20[redacted] (Rx DAY 526): PARASITES: NEGATIVE [0 - 0] UNIT NOT REPORTED; ROTAVIRUS: NEGATIVE [0 - 0] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	534
Duration of AE	11 DAYS
Severity	MODERATE

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

Event #2: Serious Adverse Event

Event Description	BRONCHIAL ASTHMA- OBSERVATION
Preferred term	喘息
AE Onset Date / Rx Day	[redacted] / 551
Age at AE Onset	[redacted]
Laboratory Testing	
[redacted] (Rx DAY 551): IGE: 345.2 [0 - 200] IU/ML	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	554
Duration of AE	4 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THE CAUSE OF CAUGH WAS PROBABLY ALLERGY. CAUGH WAS IN M11-290 AS AE. AND OCCASIONALLY BLOCKED NOSE. IF IT IS NECESSARY, I'LL ADD IT TO AE PROTOCOL M11-290
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	GROWTH FAILURE
Preferred term	成長不全
AE Onset Date / Rx Day	[redacted] / 876
Age at AE Onset	[redacted]
Laboratory Testing	

[redacted] (Rx DAY 846): CORTISOL 8.00 PM: 0.1 [2.9 - 17.3] UG/DL; GH NIGHT PROFILE: 0.576 [0 - 3] NG/ML; [redacted] (Rx DAY 847): A1C: 5.2 [4.5 - 6.2] %; FT3: 4.82 [3.7 - 10] PMOL/L; MAGNESIUM: 2.38 [1.7 - 2.1] MG/DL; RDW-CV: 17.2 [11.5 - 14.5] %; [redacted] (Rx DAY 877): ANTI-TPO: 10 [0 - 35] IU/ML; CORTISOL 8.00 AM: 0.8 [3.7 - 19.4] UG/DL; FT4: 16.2 [8.36 - 29.6] PMOL/L; GH NIGHT PROFILE: FROM 3 TO 8.84 [0 - 3] NG/ML; IG: 0.5 [0 - 0.5] %; IGF-1: 121 [111 - 551] NG/ML; MCH: 23 [26 - 34] PG; MCHC: 29 [31 - 37] G/DL; MCV: 79.2 [80 - 98] FL; MPV:

10.2 [7 - 12] FL; NRBC: 0/100WBC [0 - 0] RATIO; P-LCR: 27 [19 - 47] %; PCT: 0.5 [0.12 - 0.36] %; PDW: 11.9 [9 - 16] FL; PROLACTIN: 12.3 [2.7 - 11.8] NG/ML; RDW-SD: 49.3 [39 - 52] FL; TSH: 0.95 [0.35 - 5.5] UIU/ML; VITAMIN D3: 32.4 [0 - 100] NG/ML; [redacted]20[redacted] (Rx DAY 879): GH: FROM 0.314 TO 6.2 [0 - 3] NG/ML; [redacted]20[redacted] (Rx DAY 880): GH: 6.34 [0 - 3] NG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx DAY 920): MRI: THE CORRECT PICTURE OF THE PITUITARY GLAND

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:04:34

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，[redacted] 歳の男児（ポーランド）であり，重篤な有害事象の気管支炎を発現した。関連する病歴は，潰瘍性大腸炎による貧血，心エコー図変化を伴わない機能性雑音及び潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，気管支炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，気管支炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，脱力，咳嗽及び体温が 39°C であったため，被験者は入院した。気管支炎の診断が下され，抗生剤が投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な状態で退院した。

治療薬として Cipronex（シプロフロキサシン）及び Flukonazol（フルコナゾール）が投与された。

The patient's past medications include:

NATRII CROMOGLICAS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

VANCOMYCIN for ULCERATIVE COLITIS EXACERBATION ([redacted] 20[redacted] - [redacted] 20[redacted])

CIPROFLOXACIN for ULCERATIVE COLITIS EXACERBATION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1)　Bronchitis (10006451)　(Bronchitis (10006451))　[v.20.0]　[10006451]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of BRONCHITIS

- Investigator: Infection

- AbbVie: Not applicable

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，[redacted] 歳の男児（ポーランド）であり，重篤な有害事象の気管支喘息（観察入院）観察を発現した。関連する病歴は，過少体重，潰瘍性大腸炎，膵炎（2 回，1 回目は特発性，2 回目は免疫抑制剤の使用による）及び成長不全であった。被験者は非喫煙者及び非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は気管支炎のため入院した。

20[redacted] 年 [redacted] 月 [redacted] 日，気管支喘息（観察入院）が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，気管支喘息 - 観察は回復した。

軽度の咳嗽が断続的に数ヵ月間認められていた。20[redacted] 年 [redacted] 月 [redacted] 日，気管支喘息の観察及び予定されていた診断検査のため，被験者は入院したが，本事象に対する治療は行われなかった。肺活量測定の結果は正常であり，アレルギー検査では陰性であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

NATRII CROMOGLICAS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

Causality for HUMIRA (Open Label)

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1) Asthma bronchial (10003555) (Asthma (10003553)) [v.21.0] [10003555]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of BRONCHIAL ASTHMA- OBSERVATION

- Investigator: The cause of cough was probably allergy. Cough was in M11-290 as AE and occasionally blocked nose. If it is necessary, I'll add it to AE protocol M11-290

- AbbVie: Risk factor includes pre-existing ulcerative colitis. IBD is significantly associated with atopy when compared with matched controls. Please see citation. (refaat MM, Ahmed TM, Eldin SS, Kamal AT, Melek NA, Amin MM. Atopic manifestations I patients with inflammatory bowel disease. J Pak Med Stud. 2012; 2(3):28-34).

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BASOPHILS: 0.2 % (normal 0 to 1)

[redacted] 20[redacted] EOSINOPHILS: 0.8 % (normal 1.0 to 5.0)

[redacted] 20[redacted] HEMATOCRIT: 41.9 % (normal 37 to 41)

[redacted] 20[redacted] IGE: 345.2 IU/mL (normal 0 to 200)

[redacted] 20[redacted] LYMPHOCYTES: 12.7 % (normal 35 to 55)

[redacted] 20[redacted] MONOCYTES: 10.1 % (normal 1.0 to 6.0)

[redacted] 20[redacted] NEUTROPHILS: 76.2 % (normal 40 to 60)

[redacted] 20[redacted] PLATELET COUNT: 473 No units (normal 170 to 540)

[redacted] 20[redacted] WBC: 15.1 X10**3/MM**3 (normal 4.5 to 13)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の男児（ポーランド）であり，重篤な有害事象の成長不全を発現した。関連する病歴は，炎症性腸疾患，過少体重及び成長不全であった。
20[redacted] 年 [redacted] 月 [redacted] 日，成長不全が発現した。
20[redacted] 年 [redacted] 月から成長不全の持続が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は成長不全の診断のため入院し，臨床検査が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Omnitrope（ソマトロピン［遺伝子組み換え］）が投与された。

Causality for HUMIRA (Open Label)

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1) Growth failure (10071095) (Growth failure (10071095)) [v.21.0] [10071095]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of GROWTH FAILURE

- Investigator: Unknown

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING GROWTH FAILURE SINCE 20[redacted].

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CORTISOL 8.00 AM: 0.8 UG/DL (normal 3.7 to 19.4)

[redacted] 20[redacted] CORTISOL 8.00 PM: 0.1 UG/DL (normal 2.9 to 17.3)

[redacted] 20[redacted] EOSINOPHILS: 0.7 % (normal 1 to 5)

[redacted] 20[redacted] GH: FROM 0.314 TO 6.2 (NORMAL 0-3NG/ML)

[redacted] 20[redacted] GH NIGHT PROFILE: 0.576 NG/ML (normal 0 to 3)

[redacted] 20[redacted] GH NIGHT PROFILE: FROM 3 TO 8.84 (NORMAL 0-3NG/ML)

[redacted] 20[redacted] INORGANIC PHOSPHORUS: 3.7 mg/dL (normal 4.5 to 5.5)

[redacted] 20[redacted] LYMPHOCYTES: 20 % (normal 35 to 55)

[redacted] 20[redacted] MAGNESIUM: 2.38 mg/dL (normal 1.7 to 2.1)

[redacted] 20[redacted] MCH: 23 PG (normal 26 to 34)

[redacted] 20[redacted] MCHC: 29 G/DL (normal 31 to 37)

[redacted] 20[redacted] MCV: 79.2 FL (normal 80 to 98)

[redacted] 20[redacted] MONOCYTES: 8 % (normal 1 to 6)

[redacted] 20[redacted] MRI: the correct picture of the pituitary gland

[redacted] 20[redacted] NEUTROPHILS: 70.9 % (normal 40 to 60)

[redacted] 20[redacted] NRBC: 0/100WBC

[redacted] 20[redacted] PCT: 0.5 % (normal 0.12 to 0.36)

[redacted] 20[redacted] PLATELET COUNT: 487 X10**3/MCL (normal 140 to 440)

[redacted] 20[redacted] PROLACTIN: 12.3 NG/ML (normal 2.7 to 11.8)

[redacted] 20[redacted] RDW-CV: 17.2 % (normal 11.5 to 14.5)

[redacted] 20[redacted] RDW-SD: 49.3 FL (normal 39 to 52)

[redacted] 20[redacted] THYROXINE FREE: 16.2 mg/dL (normal 8.36 to 29.6)

[redacted] 20[redacted] TRIIODOTHYRONINE FREE: 4.82 mg/dL (normal 3.7 to 10)

[redacted] 20[redacted] TSH: 0.95 UIU/ML (normal 0.35 to 5.5)

[redacted] 20[redacted] WBC: 20.8 X10**3/MCL (normal 4 to 12)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血	X			
失血性貧血	X			
直腸出血	X			
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EOW	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
CLOTTING PROBLEMS: THROMBOCYTEMIA	20[redacted]
OTHER: CHEILITIS	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: ARTRALGIA	20[redacted]
OTHER: FATIGUE	20[redacted]

Prior Procedures	Procedure Year
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD-MSD				[redacted] / 1	[redacted] / 358	366
Adalimumab	0.67 ML	SUBCUTANEOUSLY	EOW	[redacted] / 367	[redacted] / 407	54
Adalimumab	0.66 ML	SUBCUTANEOUSLY	EOW	[redacted] / 421	[redacted] / 528	114
Adalimumab	0.68 ML	SUBCUTANEOUSLY	EOW	[redacted] / 535	[redacted] / 612	83
Adalimumab	0.72 ML	SUBCUTANEOUSLY	EOW	[redacted] / 618	[redacted] / 695	84
Adalimumab	0.68 ML	SUBCUTANEOUSLY	EOW	[redacted] / 702	[redacted] / 709	21

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
MESALAZINE	1500 mg (milligram(s))	BID	Y-M: 20[redacted] / -209
AZATHIOPRINE	12.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -114

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
MESALAZINE	1500 mg (milligram(s))	BID	Y-M: 20[redacted] / -209	ONGOING
AZATHIOPRINE	12.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -114	ONGOING
COLECALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted] / 23	ONGOING
FERRIC PYROPHOSPHATE	60 mg (milligram(s))	QD	Y-M: 20[redacted] / 242	Y-M: 20[redacted] / 618
CYANOCOBALAMIN	10 mcg (microgram(s))	QD	Y-M: 20[redacted] / 281	ONGOING
FOLIC ACID	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 281	Y-M: 20[redacted] / 618
RED BLOOD CELLS, CONCENTRATED	3 DF (dosage form)	OTHER: 3 UNITS (1 IV INFUSION ON [redacted] AND 2 IV INFUSIONS ON [redacted])	Y-M: 20[redacted] / 435	Y-M: 20[redacted] / 436
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] /

			437	500
POTASSIUM CHLORIDE	1 DF (dosage form)	QD	Y-M: 20[redacted]-[redacted] / 437	Y-M: 20[redacted]-[redacted] / 500
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 437	Y-M: 20[redacted]-[redacted] / 500
ASCORBIC ACID W/FERRIC PYROPHOSPHATE	595 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 619	Y-M: 20[redacted]-[redacted] / 702
FERROUS SULFATE	1 DF (dosage form)	TID	Y-M: 20[redacted]-[redacted] / 702	ONGOING
RED BLOOD CELLS, CONCENTRATED	3 UNITS IV INFUSION ON [redacted]20[redacted] 3 UNITS IV INFUSION ON [redacted]20[redacted]	OTHER: 3 UNITS IV INFUSION ON [redacted]20[redacted]	Y-M: 20[redacted]-[redacted] / 702	Y-M: 20[redacted]-[redacted] / 702
CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 703	ONGOING
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 703	ONGOING
POTASSIUM CHLORIDE	1 DF (dosage form)	QD	Y-M: 20[redacted]-[redacted] / 703	ONGOING
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 703	ONGOING

Event #1: Serious Adverse Event

Event Description	SEVERE BLOOD ANAEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 435
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (Rx DAY 435): Stool STOOL CULTURE (SS, CAMPYLOBACTER): Negative

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	441
Duration of AE	7 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	EXACERBATION OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	WORSENING OF THE BLOOD ANAEMIA DUE TO RECTAL BLEEDING
Preferred term	失血性貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 535
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	540
Duration of AE	6 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MODERATE COURSE OF THE ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	WORSENING OF THE BLOOD ANAEMIA DUE TO RECTAL BLEEDING
Preferred term	直腸出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 535
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	540
Duration of AE	6 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MODERATE COURSE OF THE ULCERATIVE COLITIS

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

Event #4: Serious Adverse Event

Event Description	EXACERBATION OF THE ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 700
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx DAY 702): BLOOD TRANSFUSION: IMPROVING RESULTS OF BLOOD MORPHOLOGY PARAMETERS

AE Stopped Rx Day	704
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	EXACERBATION OF THE MAIN DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:04:34

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の失血性貧血（高度）を発現した。関連する病歴は，鉄欠乏性貧血，血小板血症及び潰瘍性大腸炎であった。被験者は非喫煙者であり，飲酒の習慣はなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，失血性貧血（高度）が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，失血性貧血（高度）は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪及び失血性貧血（高度）のため，被験者は入院した。関連するリスク因子には慢性失血性貧血及び直腸出血があった。20[redacted] 年 [redacted] 月 [redacted] 日，臨床症状の消失後，被験者は退院した。

治療薬として Kalipoz-prolongatum（塩化カリウム），Helicid（オメプラゾール），Encorton 及び濃厚赤血球が投与された。

Causality for HUMIRA (Open Label)

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1) Anaemia (10002034) (Anaemia (10002034)) [v.21.1] [10002034]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of SEVERE BLOOD ANAEMIA

- Investigator: Exacerbation of ulcerative colitis.

- AbbVie: Risk factors include pre-existing iron deficiency anemia and ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HEMATOCRIT: 19 % (normal 35 to 46)

[redacted] 20[redacted] HEMATOCRIT: 31 % (normal 35 to 46)

[redacted] 20[redacted] HEMOGLOBIN: 5 G/DL (normal 12 to 16)

[redacted] 20[redacted] HEMOGLOBIN: 9.2 G/DL(normal 12 to 16)

Unknown date STOOL CULTURE: STOOL CULTURE (SS, CAMPYLOBACTER) - negative
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の直腸出血による失血性貧血の悪化が認められた。関連する病歴は，鉄欠乏性貧血，血小板血症及び広範囲の潰瘍性大腸炎／汎大腸炎であった。被験者は非喫煙者及び非アルコール摂取者であった。
20[redacted] 年 [redacted] 月 [redacted] 日，直腸出血による失血性貧血の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，直腸出血による失血性貧血の悪化は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，高度の貧血に対して輸血を受けるため，被験者は入院した。治験責任医師によると，関連するリスク因子には潰瘍性大腸炎の過程で認められた直腸出血があった。被験者の全般的な状態は良好であり，腹痛は認められなかった。排便は，血便が 1 日 2～3 回認められた。治験責任医師は，血液形態学的検査異常のアラートを受領した。濃厚赤血球の静脈内輸血が行われ，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に退院した。
治療薬として Witamina b12（シアノコバラミン）及び Acidum folicum（葉酸）が投与された。

The patient's past medications include:

KONCENTRAT KRWINEK CZERWONYCH for SEVERE ANAEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

HELICID for PREVENTION OF DIGESTIVE TRACT DURING SYSTEMIC STEROIDOTHERAPY and PREVENTION OF DIGESTIVE TRACT DURING SYSTEMIC STEROIDOTHERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

KALIPOZ-PROLONGATUM for PREVENTION OF HYPOKALEMIA DURING STEROIDOTHERAPY and PREVENTION OF HYPOKALEMIA DURING STEROIDOTHERAPY ([redacted]

[redacted] 20[redacted] - [redacted] 20[redacted])

ENCORTON for EXACERBATION OF ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Anemia aggravated (10054309) (Anaemia (10002034)) [v.22.0] [10054309]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2) Rectal bleeding (10038035) (Rectal haemorrhage (10038063)) [v.22.0] [10038035]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF THE BLOOD ANAEMIA DUE TO RECTAL BLEEDING

- Investigator:

- AbbVie: Risk factors include pre-existing iron deficiency anemia and ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HEMOGLOBIN: 6.1 G/DL (normal 12 to 16)

[redacted] 20[redacted] HEMOGLOBIN: 11.5 G/DL (normal 12 to 16)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎の増悪が認められた。関連する病歴は，鉄欠乏性貧血，血小板血症及び潰瘍性大腸炎であった。被験者は非喫煙者及び非アルコール摂取者であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日に高度の失血性貧血が認められ，20[redacted] 年 [redacted] 月 [redacted] 日には直腸出血による貧血の悪化が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は脱力及び顔面蒼白のため病院を受診した。入院時の身体的診察で失血性貧血が認められた。20[redacted] 年 [redacted] 月 [redacted] 日に濃厚赤血球 3 単位を輸血したところ，血液形態学的パラメータ値の改善がみられた。ヘモグロビン値は 10.3 g/dL に改善した。同日のその後，被験者は退院した。
治験責任医師は，（肉類を摂取せず）鉄源を有さない状態での直腸出血の持続がリスク因子であると判断した。
治療薬として Sorbifer durules（アスコルビン酸／硫酸鉄水和物），Acidum folicum（葉酸），Witamina b12（シアノコバラミン）及び Kalipoz-prolongatum（塩化カリウム）が投与された。

The patient's past medications include:

ACIDUM FOLICUM for ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

ENCORTON for EXACERBATION OF ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of EXACERBATION OF THE ULCERATIVE COLITIS

- Investigator: Exacerbation of the main disease.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALBUMIN: 4 G/L (normal 3.5 to 5.2)

[redacted] 20[redacted] HEMATOCRIT: 24.7 % (normal 37 to 47)

[redacted] 20[redacted] HEMOGLOBIN: 6.5 G/DL (normal 12 to 16)

[redacted] 20[redacted] HEMOGLOBIN: 10.3 G/DL (normal 12 to 16)

[redacted] 20[redacted] HEMOGLOBIN: 10.3 G/DL (normal 11.2 to 15.7)

[redacted] 20[redacted] PLATELET COUNT: 513 X10**3/MCL (normal 140 to 440)

[redacted] 20[redacted] RBC: 4.32 X10**6/MCL (normal 4 to 5)

[redacted] 20[redacted] WBC: 9.68 X10**3/MCL (normal 140 to 440)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EOW	1[redacted]	MALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]
SEIZURE DISORDER/CONVULSIONS: EPILEPSY	20[redacted]

Prior Procedures	Procedure Year
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD-MSD				[redacted]20[redacted] / 1	[redacted]20[redacted] / 359	365
Adalimumab	0.8 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 367	[redacted]20[redacted] / 1031	678

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	75 mg (milligram(s))	BID	Y-M: 20[redacted]
INFLIXIMAB	300 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -199
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -199
URSODEOXYCHOLIC ACID	250 mg (milligram(s))	BID	Y-M: 20[redacted] / -122

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -199	ONGOING
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -199	ONGOING
URSODEOXYCHOLIC ACID	250 mg (milligram(s))	BID	Y-M: 20[redacted] / -122	ONGOING
LEVETIRACETAM	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 1	ONGOING
PARACETAMOL	400 mg (milligram(s))	BID	Y-M: 20[redacted] / 874	Y-M: 20[redacted] / 875
CEFUROXIME	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 874	Y-M: 20[redacted] / 876
CEFUROXIME	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 876	Y-M: 20[redacted] / 887

Event #1: Serious Adverse Event

Event Description	CHOLECYSTITIS
Preferred term	胆嚢炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 874
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx DAY 874): ABDOMINAL USG: NORMAL

AE Stopped Rx Day	876
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted] 20[redacted]:04:34
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の胆嚢炎を発現した。関連する病歴は，潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎）であった。
20[redacted] 年 [redacted] 月 [redacted] 日，胆嚢炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胆嚢炎は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。胆嚢炎の疑いの経過中に腹痛が認められ，治療を行ったところ，改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬としてアセトアミノフェン及び Tarcefuoksym が投与された。

The patient's past medications include:

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

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

ENCORTON for UC FLARE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

HELICID for TOGETHER WITH ENCORTON ([redacted] 20[redacted] - [redacted] 20[redacted])

KALIPOZ for TOGETHER WITH ENCORTON ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Cholecystitis (10008612) (Cholecystitis (10008612)) [v.20.1] [10008612]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of CHOLECYSTITIS

- Investigator: Not applicable.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL USG: Normal

[redacted] 20[redacted] RBC (HEMATOLOGY): 5.19 X10**12/L

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
大腸ポリープ	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EOW	1[redacted]	MALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD-MPL-FREIND				[redacted]20[redacted] / 1	[redacted]20[redacted] / 359	365
Adalimumab	0.74 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 367	[redacted]20[redacted] / 381	28
Adalimumab	0.78 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 395	[redacted]20[redacted] / 527	140
Adalimumab	0.77 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 535	[redacted]20[redacted] / 535	6
Adalimumab	0.78 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 541	[redacted]20[redacted] / 611	78

Adalimumab	0.79 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 619	[redacted]20[redacted] / 696	84
Adalimumab	0.8 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 703	[redacted]20[redacted] / 780	84
Adalimumab	0.79 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 787	[redacted]20[redacted] / 864	84
Adalimumab	0.8 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 871	[redacted]20[redacted] / 1034	177

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
INFLIXIMAB	200 mg (milligram(s))	ACORDING TO STANDARD TREATMENT WITH INFLIXIMAB - 3 DOSES	Y-M: 20[redacted]
INFLIXIMAB	300 mg (milligram(s))	ACCORDING TO STANDARD TREATMENT WITH INFLIXIMAB - 5 DOSES	Y-M: 20[redacted]
CICLOSPORIN	100 mg (milligram(s))	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -269
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -133
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted] / -48

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -269	Y-M: 20[redacted] / 619
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted] / -48	ONGOING

Event #1: Serious Adverse Event

Event Description	COLON POLYPS
Preferred term	大腸ポリープ
AE Onset Date / Rx Day	[redacted]20[redacted] / 468
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx DAY 469): ENDOSCOPY WITH POLYPECTOMI: DURING THE COLONOSCOPY THE NUMBER

OF POLYPS WAS VISUALIZED IN TRANSVERSE AND SIGMOID COLON, TGE BIGGEST IN THE AREA OF SPLENIC FLEXURE. IN SUMMARY THE 18 PULYPS WAS REMOVED. POLYPS WAS

AE Stopped Rx Day	470
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNDERLYING DIAGNOSIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted] 20[redacted]:04:34
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の結腸ポリープを発現した。関連する病歴は，潰瘍性大腸炎であった。被験者は非喫煙者及び非アルコール摂取者であった。
20[redacted] 年 [redacted] 月 [redacted] 日，結腸ポリープが発現した。20[redacted] 年 [redacted] 月 [redacted] 日，結腸ポリープは回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，血便及び腹痛の症状のため，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，結腸内視鏡検査及びポリープ切除が行われた。ポリープは横行及び S 状結腸に認められ，最も大きいポリープは脾弯曲部にみられた。18 個のポリープが除去され，2[redacted]8 年 [redacted] 月 [redacted] 日に被験者は退院した。

The patient's past medications include:

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

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

BUDESONID MMX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of COLON POLYPS

- Investigator: Underlying diagnosis.

- AbbVie: Event is more likely related to pre-existing ulcerative colitis and prior history of polyps (20[redacted]).

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HEMATOCRIT: 31.0 % (normal 40.0 to 54.0)

[redacted] 20[redacted] HEMOGLOBIN: 9.9 G/DL (normal 14.0 to 18.0)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
卵巣嚢胞	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EOW	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]
OTHER: ACNE	20[redacted]

Prior Procedures	Procedure Year
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD-MHD				[redacted]20[redacted] / 1	[redacted]20[redacted] / 359	362
Adalimumab	0.77 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 364	[redacted]20[redacted] / 381	29
Adalimumab	0.76 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 393	[redacted]20[redacted] / 410	28
Adalimumab	0.77 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 421	[redacted]20[redacted] / 437	29

Adalimumab	0.78 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 450	[redacted]20[redacted] / 606	168
Adalimumab	0.79 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 618	[redacted]20[redacted] / 690	84
Adalimumab	0.8 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 702	[redacted]20[redacted] / 1565	877

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -218
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -218
AZATHIOPRINE	500 mg (milligram(s))	QID	Y-M: 20[redacted]-[redacted] / -195
SULFASALAZINE	500 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -110
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -89
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted]-[redacted] / -47
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / -47

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -218	Y-M: 20[redacted]-[redacted] / 1577
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted]-[redacted] / -47	ONGOING
DROSPIRENONE W/ETHINYLESTRADIOL	1 DF (dosage form)	QD	Y-M: 20[redacted]-[redacted] / 379	Y-M: 20[redacted]-[redacted] / 447
DROTAVERINE HYDROCHLORIDE	3 DF (dosage form)	QD	Y-M: 20[redacted]-[redacted] / 419	Y-M: 20[redacted]-[redacted] / 420
DALTEPARIN SODIUM	500 IU (international unit(s))	QD	Y-M: 20[redacted]-[redacted] / 891	Y-M: 20[redacted]-[redacted] / 891
CEFAZOLIN	1 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / 891	Y-M: 20[redacted]-[redacted] / 892
MORPHINE SULFATE	10 mg (milligram(s))	OTHER: 5 TIMES DAILY	Y-M: 20[redacted]-[redacted] / 892	Y-M: 20[redacted]-[redacted] / 892

Event #1: Serious Adverse Event

Event Description	RIGHT OVARIAN CYST
Preferred term	卵巣嚢胞
AE Onset Date / Rx Day	[redacted]20[redacted] / 419
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	

Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	420
Duration of AE	2 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	WORSENING OF THE LEFT OVARIAN CYS
Preferred term	卵巣嚢胞
AE Onset Date / Rx Day	[redacted]20[redacted] / 891
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx DAY 891): TRANSVAGINAL USG: IN THE LEFT OVARY PROJECTION (BEHIND THE UTERUS) VISIBLE THE CHANGE WITH A DIAMETER OF 5 CM; [redacted]20[redacted] (Rx DAY 892): LAPARATOMY: RESECTION OF LEFT OVARIAN CYST	
AE Stopped Rx Day	893
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:04:34
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の右卵巣嚢胞及び左卵巣嚢胞の悪化が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，右卵巣嚢胞が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右卵巣嚢胞は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，左卵巣嚢胞の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，左卵巣嚢胞の悪化は回復した。

20[redacted] 年 [redacted] 月に非重篤な有害事象の卵巣嚢胞が発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腹痛のため入院し，右卵巣嚢胞の悪化と診断された。同日の婦人科の超音波検査で右卵巣嚢胞が認められた。薬剤が投与され，症状の軽快がみられた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な有害事象の卵巣嚢胞は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，超音波検査が行われ，卵巣嚢胞の大きさに変化が認められたが，臨床症状はみられなかった。同日，左卵巣嚢胞の悪化のため，被験者は入院した。その他の症状は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，開腹及び左卵巣嚢胞の切除が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Exacyl（トラネキサム酸），Fragmin（ダルテパリンナトリウム），Biofazolin（セファゾリンナトリウム），Rigevidon（レボノルゲストレル・エチニルエストラジオール），Morphini Sulfas Wzf（モルヒネ硫酸塩水和物），NO-Spa，Sidretella（ドロスピレノン・エチニルエストラジオール）及び Drotaverini Hydrochloridum が投与された。

Causality for HUMIRA (Open Label)

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1) Ovarian cyst (10033132) (Ovarian cyst (10033132)) [v.20.1] [10033132]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2) Ovarian cyst (10033132) (Ovarian cyst (10033132)) [v.20.1] [10033132]

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

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

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of RIGHT OVARIAN CYST

- Investigator: Not applicable.

- AbbVie: A common gynecological complication.

Event of WORSENING OF LEFT OVARIAN CYST

- Investigator: Not applicable.

- AbbVie: Ovarian cysts are common in the general female population.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] TRANSVAGINAL USG: In the left ovary projection (behind the uterus) visible the change with a diameter of 5cm.

[redacted] 20[redacted] ultrasound: right ovarian cyst

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EOW	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
Ulcerative colitis	20[redacted]

Prior Procedures	Procedure Year
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ISD-MSD				[redacted]20[redacted] / 1	[redacted]20[redacted] / 359	364
Adalimumab	0.8 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 365	[redacted]20[redacted] / 436	85
Adalimumab	0.79 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 450	[redacted]20[redacted] / 520	84
Adalimumab	0.74 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 535	[redacted]20[redacted] / 604	83
Adalimumab	0.78 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 618	[redacted]20[redacted] / 688	84

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	75 mg (milligram(s))	50 MG + 25 MG	Y-M: 20[redacted]
MERCAPTOPURINE	75 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted]
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -252
MYCOPHENOLATE MOFETIL	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -218
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -105
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -105

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted]	ONGOING
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -105	ONGOING
FERROUS GLUCONATE	NA DF (dosage form)	OTHER: AS NEEDED	Y-M: 20[redacted] / 547	Y-M: 20[redacted] / 560

Event #1: Serious Adverse Event

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 528
Age at AE Onset	1[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx DAY 555): COLONOSCOPY: MAYO 2 - THROUGHOUT THE ENTIRE EXPLORED COLON THE MUCOSA SEEN FRAGMENTARILY: LOSS OF VASCULAR DRAWING, GRANULARITY, FRIABILITY, MINOR EROSIONS	
AE Stopped Rx Day	620
Duration of AE	93 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNDERLYING DIAGNOSIS

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

Generated: [redacted] 20[redacted]:04:34
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の貧血が発現した。関連する病歴は，潰瘍性大腸炎であった。被験者は非喫煙者及び非アルコール摂取者であった。
20[redacted] 年 [redacted] 月 [redacted] 日，貧血が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，ヘモグロビン及びヘマトクリット低値の徴候及び症状のため，被験者は入院した。Ferrum（フマル酸第一鉄）が静脈内投与されたが，ヘモグロビン値はほとんど改善しなかった。20[redacted] 年 [redacted] 月 [redacted] 日に実施された結腸内視鏡検査の結果，血管は描出されず，粘膜は顆粒状及び脆弱で，わずかなびらんが認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Ferrum（フマル酸第一鉄）が投与された。

The patient's past medications include:

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

MERCAPTOPURINUM VIS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

MYCOPHENOLATE MOFETIL for ULCERATIVE COLITIS [redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for HUMIRA (Open Label)

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1) Anemia (10002272) (Anaemia (10002034)) [v.21.0] [10002272]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ANEMIA

- Investigator: Underlying diagnosis.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] COLONOSCOPY: MAYO 2 - THROUGHOUT THE ENTIRE EXPLORED COLON THE MUCOSA SEEN FRAGMENTARILY: LOSS OF VASCULAR DRAWING, GRANULARITY, FRIABILITY, MINOR EROSIONS

[redacted] 20[redacted] HEMATOCRIT: 32.2 % (normal 37 to 47)

[redacted] 20[redacted] HEMATOCRIT: 28.9 % (normal 37 to 47)

[redacted] 20[redacted] HEMATOCRIT: 32.9 % (normal 37 to 47)

[redacted] 20[redacted] HEMATOCRIT: 30.7 % (normal 37 to 47)

[redacted] 20[redacted] HEMATOCRIT: 32 % (normal 37 to 47)

[redacted] 20[redacted] HEMOGLOBIN: 8.2 G/DL (normal 12 to 16)

[redacted] 20[redacted] HEMOGLOBIN: 8.2 G/DL (normal 12 to 16)

[redacted] 20[redacted] HEMOGLOBIN: 7.1 G/DL (normal 12 to 16)

[redacted] 20[redacted] HEMOGLOBIN: 7.9 G/DL (normal 12 to 16)

[redacted] 20[redacted] HEMOGLOBIN: 8.3 G/DL (normal 12 to 16)

Subject [redacted] (Investigator[redacted]

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
上肢骨折	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EOW	[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: HB 7.3G/DL	20[redacted]
Ulcerative colitis	20[redacted]
OTHER: POSITIVE QUANTIFERON TEST	20[redacted]

Prior Procedures	Procedure Year
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD-MHD				[redacted]20[redacted] / 1	[redacted]20[redacted] / 357	364
Adalimumab	0.2 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 365	[redacted]20[redacted] / 378	27
Adalimumab	0.22 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] /	[redacted]20[redacted] /	28

Adalimumab	0.23 ML	SUBCUTANEOUSLY	EOW	393 [redacted]20[redacted] / 421	407 [redacted]20[redacted] / 602	195
Adalimumab	0.24 ML	SUBCUTANEOUSLY	EOW	[redacted]20[redacted] / 617	[redacted]20[redacted] / 742	139

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	25 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -220

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
AZATHIOPRINE	25 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -220	ONGOING
PARACETAMOL	500 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 444	Y-M: 20[redacted]-[redacted] / 444

Event #1: Serious Adverse Event

Event Description	FRACTURE OF THE LEFT ELBOW BONE.
Preferred term	上肢骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 444
Age at AE Onset	[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx DAY 444): X-RAY: ELBOW BONE FRACTURE LEFT; PLASTER DRESSING:

AE Stopped Rx Day	489
Duration of AE	46 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MECHANICAL INJURY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	PERSIST OR SIGNIF DISABILITY/INCAPACITY, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]20[redacted]:04:34

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，[redacted]歳の男児（ポーランド）であり，重篤な有害事象の左尺骨骨折を発現した。
20[redacted]年[redacted]月[redacted]日，左尺骨骨折が発現した。
被験者は転倒し，左手に痛みを覚えた。腫脹及び疼痛が認められた。左手首及び肘の X 線検査が実施され，左尺骨骨折がみられた。ドレッシングプラスターによる固定が行われた。20[redacted]年[redacted]月[redacted]日，左尺骨骨折は回復した。
治療薬としてアセトアミノフェンが投与された。

Causality for HUMIRA (Open Label)

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1) Elbow fracture (10014344) (Upper limb fracture (10061394)) [v.21.1] [10014344]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of FRACTURE OF THE LEFT ELBOW BONE

- Investigator: Mechanical injury.

- AbbVie: Event is more likely related to injury sustained from a fall.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] X-RAY: elbow bone fracture left

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EOW	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: IBD	20[redacted]
Ulcerative colitis	20[redacted]
OSTEOPENIA: BONE DENSITY DECREASE (DENSITOMETRY)	20[redacted]
ANEMIA: SIDEROPENIC	20[redacted]

Prior Procedures	Procedure Year
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD-MSD-FNREIND				[redacted] / 1	[redacted] / 360	366
Adalimumab	0.37 ML	SUBCUTANEOUSLY	EOW	[redacted] / 368	[redacted] / 437	83
Adalimumab	0.38 ML	SUBCUTANEOUSLY	EOW	[redacted] / 451	[redacted] / 521	84
Adalimumab	0.34 ML	SUBCUTANEOUSLY	EOW	[redacted] / 535	[redacted] / 591	70

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -290
PREDNISONE	30 mg (milligram(s))	BID	Y-M: 20[redacted] / -290
ESCHERICHIA COLI	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -245
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -245
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -245
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -121

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
ESCHERICHIA COLI	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -245	ONGOING
FOLIC ACID	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -245	ONGOING
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / -245	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -121	ONGOING
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 564	Y-M: 20[redacted] / 577
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 578	Y-M: 20[redacted] / 591
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 592	Y-M: 20[redacted] / 609
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 598	ONGOING
PARACETAMOL	400 mg (milligram(s))	TID	Y-M: 20[redacted] / 598	Y-M: 20[redacted] / 605
CIPROFLOXACIN HYDROCHLORIDE	280 mg (milligram(s))	BID	Y-M: 20[redacted] / 599	Y-M: 20[redacted] / 608
FLUCONAZOLE	170 mg (milligram(s))	QD	Y-M: 20[redacted] / 599	Y-M: 20[redacted] /

				608
METRONIDAZOLE	210 mg (milligram(s))	TID	Y-M: 20[redacted] / 599	Y-M: 20[redacted] / 608
TRANSFER FACTOR	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 603	Y-M: 20[redacted] / 608
CALCIUM CARBONATE	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 604	ONGOING
COLECALCIFEROL	2 gtt (drop(s))	QD	Y-M: 20[redacted] / 604	ONGOING
CIPROFLOXACIN HYDROCHLORIDE	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 609	ONGOING
FLUCONAZOLE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 609	ONGOING
METRONIDAZOLE	250 mg (milligram(s))	TID	Y-M: 20[redacted] / 609	ONGOING
PARACETAMOL	375 mg (milligram(s))	OTHER: IN CASE OF FEBRIS	Y-M: 20[redacted] / 609	Y-M: 20[redacted] / 610
BACTRIM	480 mg (milligram(s))	OTHER: BID 3 TIMES PER WEEK	Y-M: 20[redacted] / 611	ONGOING
METHYLPREDNISOLONE SODIUM SUCCINATE	250 mg (milligram(s))	QD	Y-M: 20[redacted] / 611	Y-M: 20[redacted] / 613

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

Event Description	COLITIS ULCEROSA RELAPS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 597 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (Rx DAY 597): Stool CL. DIFFICILE TEST: Negative; Blood CULTIVATION: Negative; Other RECTAL SWAB RECTAL SWAB: Negative; Other THROAT SWAB THROAT SWAB: Negative; Urine CULTIVATION: Negative

SAE Supplemental Procedure

[redacted]20[redacted](Rx DAY 598): X-RAY OF LUNGS: NEGAT.

AE Stopped Rx Day	614 (23 DAYS AFTER LAST TREATMENT)
Duration of AE	18 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNDERLYING UC DISEASE STATE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted] 20[redacted]:04:34
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の女児（スロバキア共和国）であり，重篤な有害事象の潰瘍性大腸炎の再発が認められた。関連する病歴は，炎症性腸疾患及び潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再発が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再発は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，発熱，血便及び C 反応性たん白高値のため，被験者は入院した。Solu-medrol（メチルプレドニゾロンコハク酸エステルナトリウム）が静脈内投与され，被験者の状態は改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Paralen（アセトアミノフェン），Perfalgan（アセトアミノフェン），Medoflucon（フルコナゾール），Diflucan（フルコナゾール），Entizol（メトロニダゾール），メトロニダゾール，Solu-medrol（メチルプレドニゾロンコハク酸エステルナトリウム）及び Ciprinol（シプロフロキサシン塩酸塩水和物）が投与された。

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of COLITIS ULCEROSA RELAPS

- Investigator: UNDERLYING UC DISEASE STATE

- AbbVie: A COMMON COMPLICATION OF THE UNDERLYING UC

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] high sensitivity c reactive protein: 14.48 mg/dL (normal 0.00 to 0.5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 8.72 mg/dL (normal 0 to 0.5)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EW	1[redacted]	MALE	ASIAN

Medical History	Onset Year
Ulcerative colitis	20[redacted]
OTHER: RHINITIS ALLERGIC	20[redacted]

Prior Procedures	Procedure Year
Ulcerative Colitis Disease History: Colonoscopy	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
Chewing tobacco	NEVER			
Cigarettes	NEVER			
Cigars	NEVER			
Pipes	NEVER			

Alcohol Use	Status	Number/Day
Alcohol	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
IHD-MHD-FNREIND				[redacted]20[redacted] / 1	[redacted]20[redacted] / 358	363
Adalimumab	0.8 ML	SUBCUTANEOUSLY	EW	[redacted]20[redacted] / 365	[redacted]20[redacted] / 711	360

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
MESALAZINE	1600 mg (milligram(s))	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]
EPINASTINE HYDROCHLORIDE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -26

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
MESALAZINE	1600 mg (milligram(s))	BID	Y-M: 20[redacted]	ONGOING
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 775
PREDNISOLONE VALEROACETATE APPLICATION APPLICATION	APPLICATION	BID	Y-M: 20[redacted] / 535	ONGOING
NADIFLOXACIN APPLICATION APPLICATION	APPLICATION	QD	Y-M: 20[redacted] / 535	Y-M: 20[redacted] / 692
VALISONE-G APPLICATION APPLICATION	APPLICATION	QD	Y-M: 20[redacted] / 692	ONGOING
LEVOCETIRIZINE DIHYDROCHLORIDE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 692	Y-M: 20[redacted] / 702
PYRIDOXAL PHOSPHATE	10 mg (milligram(s))	TID	Y-M: 20[redacted] / 692	Y-M: 20[redacted] / 702
PREDNISOLONE	15 mg (milligram(s))	BID	Y-M: 20[redacted] / 692	Y-M: 20[redacted] / 722
ALFACALCIDOL	0.5 mcg (microgram(s))	QD	Y-M: 20[redacted] / 692	Y-M: 20[redacted] / 773
FAMOTIDINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 692	Y-M: 20[redacted] / 773
MAGNESIUM CITRATE	50 g (gram(s))	QD	Y-M: 20[redacted] / 714	Y-M: 20[redacted] / 714
SOLITA-T1	200 mL (millilitre(s))	BID	Y-M: 20[redacted] / 715	Y-M: 20[redacted] / 715
PARACETAMOL	400 mg (milligram(s))	PRN	Y-M: 20[redacted] / 715	Y-M: 20[redacted] / 716
PREDNISOLONE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / 723	Y-M: 20[redacted] / 727
INFLIXIMAB	300 mg (milligram(s))	QD	Y-M: 20[redacted] / 724	Y-M: 20[redacted] / 724
PREDNISOLONE	15 mg (milligram(s))	BID	Y-M: 20[redacted] / 728	Y-M: 20[redacted] / 731
PREDNISOLONE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / 732	Y-M: 20[redacted] / 736
PREDNISOLONE	7.5 mg (milligram(s))	BID	Y-M: 20[redacted] / 737	Y-M: 20[redacted] / 743
PREDNISOLONE	5 mg (milligram(s))	BID	Y-M: 20[redacted] / 744	Y-M: 20[redacted] / 751
CLOBETASONE BUTYRATE APPLICATION APPLICATION	APPLICATION	QD	Y-M: 20[redacted] / 752	ONGOING
TRIAMCINOLONE ACETONIDE APPLICATION APPLICATION	APPLICATION	PRN	Y-M: 20[redacted] / 752	ONGOING
VALACICLOVIR HYDROCHLORIDE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 752	Y-M: 20[redacted] / 766

PREDNISOLONE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / 752 Y-M: 20[redacted] / 772
PARACETAMOL	400 mg (milligram(s))	PRN	Y-M: 20[redacted] / 766 ONGOING
PYRIDOXAL PHOSPHATE	10 mg (milligram(s))	TID	Y-M: 20[redacted] / 766 Y-M: 20[redacted] / 773
TRANEXAMIC ACID	250 mg (milligram(s))	TID	Y-M: 20[redacted] / 766 Y-M: 20[redacted] / 773
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2.5 g (gram(s))	TID	Y-M: 20[redacted] / 766 Y-M: 20[redacted] / 773
LIDOCAINE	6 mL (millilitre(s))	PRN	Y-M: 20[redacted] / 766 Y-M: 20[redacted] / 780
ACICLOVIR	1200 mg (milligram(s))	TID	Y-M: 20[redacted] / 773 Y-M: 20[redacted] / 775
PREDNISOLONE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / 773 Y-M: 20[redacted] / 776
AMPICILLIN	3 g (gram(s))	QID	Y-M: 20[redacted] / 773 Y-M: 20[redacted] / 778
MEROPENEM	1.5 g (gram(s))	QID	Y-M: 20[redacted] / 773 Y-M: 20[redacted] / 780
ACICLOVIR	600 mg (milligram(s))	TID	Y-M: 20[redacted] / 775 Y-M: 20[redacted] / 780
PREDNISOLONE	20 mg (milligram(s))	TID	Y-M: 20[redacted] / 777 Y-M: 20[redacted] / 780
PREDNISOLONE	30 mg (milligram(s))	BID	Y-M: 20[redacted] / 781 ONGOING
CLARITHROMYCIN	200 mg (milligram(s))	BID	Y-M: 20[redacted] / 781 Y-M: 20[redacted] / 787

Event #1: Serious Adverse Event

Event Description	AGGRAVATION OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 722 (11 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx DAY 722): CRP: 0.38 [NOT REPORTED - 0.14] MG/DL; ESR 1HOUR: 32.0 [NOT REPORTED - NOT REPORTED] MM; ESR 2HOUR: 60.0 [NOT REPORTED - NOT REPORTED] MM; ESR 30MIN: 11.0 [NOT REPORTED - NOT REPORTED] MM; [redacted]20[redacted] (Rx DAY 723): CRP: 8.88 [NOT REPORTED - 0.14] MG/DL; [redacted]20[redacted] (Rx DAY 724): CRP: 7.90 [NOT REPORTED - 0.14] MG/DL; [redacted]20[redacted] (Rx DAY 727): CRP: 1.10 [NOT REPORTED - 0.14] MG/DL; ESR 1HOUR: 51.0 [NOT REPORTED - NOT REPORTED] MM; ESR 2HOUR: 81.0 [NOT REPORTED - NOT REPORTED] MM; ESR 30MIN: 23.0 [NOT REPORTED - NOT REPORTED] MM; [redacted]20[redacted] (Rx DAY 731): CRP: 0.34 [NOT REPORTED - 0.14] MG/DL; ESR 1HOUR: 41.0 [NOT REPORTED - NOT REPORTED] MM; ESR 2HOUR: 71.0 [NOT REPORTED - NOT REPORTED] MM; ESR 30MIN: 15.0 [NOT REPORTED - NOT REPORTED] MM

Microbiology

[redacted]20[redacted] (Rx DAY 722): Stool STOOL CULTURE: Negative; Other NASAL MUCOSA INFLUENZA: Negative; [redacted]20[redacted] (Rx DAY 723): Urine URINE CULTURE: Negative; Blood BLOOD CULTURE: Negative; Other NASAL MUCOSA INFLUENZA: Negative; [redacted]20[redacted] (Rx DAY 724): Blood CMV ANTIGEN(C7-HRP): Negative

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	733 (22 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	MODERATE

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

Event #2: Serious Adverse Event

Event Description	SEPSIS
Preferred term	敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 773 (62 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx DAY 773): AMMONIA: 63 [12 - 66] MCG/DL; APTT: 45.8 [24 - 39] SEC; BASED EXESS: 0.6 [-2 - 2] MMOL/L; CHLORIDE: 95 [101 - 108] MMOL/L; CRP: 10.40 [NOT REPORTED - 0.14] MG/DL; CSF GLUCOSE: 74 [50 - 75] MG/DL; ESR 1HOUR: 48.0 [2 - 10] MM; FDP: 20.0 [NOT REPORTED - 5] MCG/ML; FERRITIN: 112.0 [15 - 160] NG/ML; FIBRINOGEN: 483 [200 - 400] MG/DL; HCO3: 26.4 [22 - 26] MMOL/L; IL2R: 672 [121 - 613] U/ML; MYCOPLASMA ANTIBODY: 80 [0 - 40] TIMES; PCO2: 47.7 [35 - 45] MMHG; PH: 7.364 [7.35 - 7.45] NO UNIT; PROCALCITONIN: 47.41 [NOT REPORTED - 0.5] NG/ML; PT-TIME: 17.6 [NOT REPORTED - NOT REPORTED] SEC; [redacted]20[redacted] (Rx DAY 774): APTT: 51.7 [24 - 39] SEC; CHLORIDE: 99 [101 - 108] MMOL/L; CRP: 14.79 [NOT REPORTED - 0.14] MG/DL; FDP: 16.5 [NOT REPORTED - 5] MCG/ML; FIBRINOGEN: 556 [200 - 400] MG/DL; PT-TIME: 14.8 [NOT REPORTED - NOT REPORTED] SEC; [redacted]20[redacted] (Rx DAY 775): CHLORIDE: 106 [101 - 108] MMOL/L; CRP: 8.07 [NOT REPORTED - 0.14] MG/DL; [redacted]20[redacted] (Rx DAY 776): APTT: 41.3 [24 - 39] SEC; B.E: -0.3 [-2 - 2] MMOL/L; CHLORIDE: 105 [101 - 108] MMOL/L; CRP: 4.79 [NOT REPORTED - 0.14] MG/DL; FDP: 13.6 [NOT REPORTED - 5] MCG/ML; FIBRINOGEN: 500 [200 - 400] MG/DL; HCO3: 24.9 [22 - 26] MMOL/L; PCO2: 43.2 [35 - 45] MMHG; PH: 7.379 [7.35 - 7.45] NO UNIT; PT-TIME: 11.1 [NOT REPORTED - NOT REPORTED] SEC; [redacted]20[redacted] (Rx DAY 778): CHLORIDE: 103 [101 - 108] MMOL/L; CRP: 1.25 [NOT REPORTED - 0.14] MG/DL; [redacted]20[redacted] (Rx DAY 780): CHLORIDE: 102 [101 - 108] MMOL/L; CRP: 0.51 [NOT REPORTED - 0.14] MG

Microbiology

[redacted]20[redacted] (Rx DAY 773): Other SPINAL FLUID , PHARYNGEAL SWAB HSV: Negative; Other SPINAL FLUID , PHARYNGEAL SWAB CMV: Negative; Other CEREBROSPINAL FULID CEREBROSPINAL FULID EXAMINATION: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx DAY 773): ELECTROENCEPHALOGRAM TEST: NON CLINICAL SIGNIFICANCE; BRAIN MRI: NON CLINICAL SIGNIFICANCE

AE Stopped Rx Day	789 (78 DAYS AFTER LAST TREATMENT)
Duration of AE	17 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	AGGRAVATION OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 778 (67 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx DAY 778): CRP: 1.25 [NOT REPORTED - 0.14] MG/DL; [redacted]20[redacted] (Rx DAY 780): CRP: 0.51 [NOT REPORTED - 0.14] MG/DL; ESR 1HOUR: 51.0 [2 - 10] MM; ESR 2HOUR: 83.0 [NOT REPORTED - NOT REPORTED] MM; ESR 30MIN: 20.0 [NOT REPORTED - NOT REPORTED] MM; [redacted]20[redacted] (Rx DAY 781): CRP: 1.16 [NOT REPORTED - 0.14] MG/DL; [redacted]20[redacted] (Rx DAY 782): CRP: 3.44 [NOT REPORTED - 0.14] MG/DL; [redacted]20[redacted] (Rx DAY 783): CRP: 2.21 [NOT REPORTED - 0.14] MG/DL; ESR 1HOUR: 56.0 [2 - 10] MM; ESR 2HOUR: 88.0 [NOT REPORTED - NOT REPORTED] MM; ESR 30MIN: 24.0 [NOT REPORTED - NOT REPORTED] MM; [redacted]20[redacted] (Rx DAY 785): CRP: 0.98 [NOT REPORTED - 0.14] MG/DL; ESR 1HOUR: 59.0 [2 - 10] MM; ESR 2HOUR: 98.0 [NOT REPORTED - NOT REPORTED] MM; ESR 30MIN: 26.0 [NOT REPORTED - NOT REPORTED] MM; [redacted]20[redacted] (Rx DAY 787): CRP: 0.77 [NOT REPORTED - 0.14] MG/DL; ESR 1HOUR: 58.0 [2 - 10] MM; ESR 2HOUR: 88.0 [NOT REPORTED - NOT REPORTED] MM; ESR 30MIN: 24.0 [NOT REPORTED - NOT REPORTED] MM

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	789 (78 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT EFFICACY WITH INFLIXIMAB
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:04:34

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の男性（日本）であり，重篤な有害事象の潰瘍性大腸炎の増悪が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，発熱，脱水，血便及び下痢の徴候及び症状が認められ，腸管粘膜の評価及びインフリキシマブの投与を開始するため，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，経口摂取は減少した。発熱に対し，治療が行われた。原疾患及び複数の免疫抑制剤による感染症が原因であると考えられた。20[redacted] 年 [redacted] 月 [redacted] 日，インフリキシマブが投与された。体温は 36.0°C であった。下痢及び血便の症状は軽快し，排便回数は減少した。血液，尿及び便培養で臨床的意義のある結果はみられなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Calonal（アセトアミノフェン），Predonine（プレドニゾロンコハク酸エステルナトリウム）及び Remicade（インフリキシマブ）が投与された。

The patient's past medications include:

ALESION for RHINITIS ALLERGIC ([redacted] 20[redacted] - [redacted] 20[redacted])

FAMOTIDINE D for PREVENTION OF GASTRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of AGGRAVATION OF UC

- Investigator: UC

- AbbVie: The underlying disorder, UC

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALBUMIN: 3.19 G/DL (normal 4.10 to 5.10)

[redacted] 20[redacted] CRP: 0.38 mg/dl

[redacted] 20[redacted] CRP: 8.88 No units

[redacted] 20[redacted] ESR 1 HR: 32.0 MM

[redacted] 20[redacted] ESR 30MIN: 15.0 no units

[redacted] 20[redacted] HEMOGLOBIN: 12.2 G/DL (normal 13.7 to 16.8)

[redacted] 20[redacted] HEMOGLOBIN: 11.4 G/DL (normal 13.7 to 16.8)

[redacted] 20[redacted] INFLUNEZA TEST: Negative

[redacted] 20[redacted] INFLUNEZA TEST: Negative

[redacted] 20[redacted] STOOL CULTURE: Negative

[redacted] 20[redacted] URINE CULTURE: Negative

[redacted] 20[redacted] WBC: 6.1 X10**3/MCL (normal 3.3 to 8.6)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M10-870

本被験者は，1[redacted] 歳の男性（日本）であり，重篤な有害事象の敗血症及び潰瘍性大腸炎の増悪が認められた。関連する病歴は，潰瘍性大腸炎であった。

被験者においては，20[redacted] 年 [redacted] 月 [redacted] 日に本試験でのアダリムマブ投与が開始されたが，本試験に参加する前の 20[redacted] 年 [redacted] 月 [redacted] 日にアダリムマブの初回投与が行われた。

20[redacted] 年 [redacted] 月 [redacted] 日，敗血症が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，敗血症及び潰瘍性大腸炎の増悪は回復した。

被験者は 20[redacted] 年 [redacted] 月 [redacted] 日～20[redacted] 年 [redacted] 月 [redacted] 日に試験に参加した。

20[redacted] 年 [redacted] 月 [redacted] 日，20[redacted] 年 [redacted] 月 [redacted] 日及び 20[redacted] 年 [redacted] 月 [redacted] 日にインフリキシマブが投与されたが，血便及び下痢は回復しなかった。20[redacted] 年 [redacted] 月 [redacted] 日の夜，被験者は体調不良となり，発熱を伴い風呂場で倒れているところを発見された（意識障害あり）。被験者は，20[redacted] 年 [redacted] 月 [redacted] 日の朝に地域の病院に搬送され，同日のその後，治験実施施設へ搬送された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。到着時，体温は 40°C であり，意識障害が認められた（GCS11:E3V4M4）。血液検査の結果，C 反応性たん白は 10.40 mg/dL，プロカルシトニンは 47 ng/mL であり，細菌感染が疑われた。

意識障害が持続していたため，髄膜炎，脳炎及び脳症が疑われ，脳髄液検査，脳電図及び脳 MRI 検査が実施された。脳電図及び脳 MRI 検査の結果，これらの可能性は除外された。

20[redacted] 年 [redacted] 月 [redacted] 日，敗血症と考えられ，メロペネム水和物及びアンピシリンの投与が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，発熱及び意識状態に改善が認められ始めた。症状が抗生剤投与により改善したことから，敗血症が原因であると考えられた。

原疾患に対してインフリキシマブ，アザチオプリン及びプレドニゾロンが投与されたことにより，被験者は易感染性状態となり，ヘルペス脳炎の可能性を否定できなかった。このため，アシクロビルの投与が開始された。しかしながら，ポリメラーゼ連鎖反応検査の結果，単純ヘルペスウイルス及びサイトメガロウイルス感染は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，抗生剤及び抗ウイルス薬の投与は継続された。被験者は解熱し，意識状態は清明となった。

（発熱，脱水，血便及び下痢の徴候及び症状が認められ，潰瘍性大腸炎の増悪のため入院している間，）プレドニゾロン 40 mg/日の投与は絶食下での点滴投与及び輸血による管理に変更された。解熱により意識清明となった後，入院前の原疾患の状態は，小児潰瘍性大腸炎活動性指標（PUCAI）75 の重症と評価された。絶食下にも関わらず，1 日 5 回の排便が持続しており，血便に近い状態であった。20[redacted] 年 [redacted] 月 [redacted] 日にプレドニゾロン 40 mg/日の投与が 60 mg/日に変更された後，排便回数は減少し，20[redacted] 年 [redacted] 月 [redacted] 日に PUCAI は 35 の中等症に改善した。その後 10 日間以上この状態が続き，食物の経口摂取を再開後も悪化は認められなかった。

血液検査における炎症反応に改善がみられた。20[redacted] 年 [redacted] 月 [redacted] 日，血液及び脳髄液の培養検査で臨床的意義のある結果はみられず，抗生剤及び抗ウイルス薬の投与は中止された。20[redacted] 年 [redacted]

月 [redacted] 日，発熱が再発し，抗生剤の投与が再開された。20[redacted] 年 [redacted] 月 [redacted] 日に発熱は回復し，再発は認められなかった。その後，血液検査で炎症反応はみられなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Predonine（プレドニゾロンコハク酸エステルナトリウム），Vicclox（アシクロビル），Viccillin（アンピシリンナトリウム），Meropen（メロペネム水和物）及び Clarith（クラリスロマイシン）が投与された。

Causality for HUMIRA (Open Label)

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1) Sepsis (10040047) (Sepsis (10040047)) [v.20.0] [10040047]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of SEPSIS

- Investigator: Infection

- AbbVie: An infection.

Event of AGGRAVATION OF UC

- Investigator: Not efficacy with Infliximab.

- AbbVie: The underlying disorder UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALBUMIN: 2.90 G/DL (normal 4.10 to 5.10)

[redacted] 20[redacted] ALBUMIN: 2.53 G/DL

[redacted] 20[redacted] APTT: 45.8 SEC (normal 24.0 to 39.0)

[redacted] 20[redacted] APTT: 41.3 SEC (normal 24.0 to 39.0)

[redacted] 20[redacted] BRAIN MRI: NON CLINICAL SIGNIFICANCE

[redacted] 20[redacted] BUN: 21.2 mg/dL (normal 8.0 to 20.0)

[redacted] 20[redacted] BUN: 17.0 mg/dL

[redacted] 20[redacted] CALCIUM: 7.59 mg/dL (normal 8.80 to 10.10)

[redacted] 20[redacted] CALCIUM: 8.27 mg/dL

[redacted] 20[redacted] CHLORIDE: 95 MMOL/L (normal 101 to 108)

[redacted] 20[redacted] CHLORIDE: 103 MMOL/L

[redacted] 20[redacted] CMV IGM ANTIBODY: Spinal fluid, pharyngeal swab: Negative

[redacted] 20[redacted] CREATININE: 1.14 mg/dL (normal 0.65 to 1.07)

[redacted] 20[redacted] CREATININE: 0.82 mg/dL

[redacted] 20[redacted] CRP: 10.40 mg/dL (normal <0.14)

[redacted] 20[redacted] CRP: 4.79 mg/dL

[redacted] 20[redacted] CRP: 1.25 mg/dL

[redacted] 20[redacted] CSF TEST: Cerebrospinal fluid examination

[redacted] 20[redacted] ELECTROENCEPHALOGRAM: NON CLINICAL SIGNIFICANCE

[redacted] 20[redacted] ERYTHROCYTE SEDIMENTATION RATE: 48.0 at 1 hr / MM (normal 2.0 to 10.0)

[redacted] 20[redacted] FDPS: 20.0 MCG/ML (normal <5.0)

[redacted] 20[redacted] FDPS: 13.6 G/DL (normal <5.0)

[redacted] 20[redacted] FIBRINOGEN: 483 mg/dL (normal 200 to 400)

[redacted] 20[redacted] FIBRINOGEN: 500 mg/dL (normal 200 to 400)

[redacted] 20[redacted] GLUCOSE: 105 mg/dL (normal 73 to 109)

[redacted] 20[redacted] GLUCOSE: 132 mg/dL

[redacted] 20[redacted] GLUCOSE: 117 mg/dL

[redacted] 20[redacted] HCO3: 26.4 MMOL/L (normal 22.0 to 26.0)

[redacted] 20[redacted] HEMATOCRIT: 34.0 % (normal 40.7 to 50.1)

[redacted] 20[redacted] HEMATOCRIT: 29.4 % (normal 40.7 to 50.1)

[redacted] 20[redacted] HEMOGLOBIN: 11.1 G/DL (normal 13.7 to 16.8)

[redacted] 20[redacted] HEMOGLOBIN: 9.5 G/DL (normal 13.7 to 16.8)

[redacted] 20[redacted] HERPES SIMPLEX ANTIBODY: Spinal fluid, pharyngeal swab: Negative

[redacted] 20[redacted] IL-2 RECEPTOR ASSAY: 672 U/ML (normal 121 to 613)

[redacted] 20[redacted] PCO2: 47.7 MMHG (normal 35.0 to 45.0)

[redacted] 20[redacted] PLATELET COUNT: 211 X10**3/MCL (normal 158 to 348)

[redacted] 20[redacted] PLATELET COUNT: 187 X10**3/MCL (normal 158 to 348)

[redacted] 20[redacted] POTASSIUM: 3.3 MMOL/L (normal 3.6 to 4.8)

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

[redacted] 20[redacted] PROCALCITONIN: 47.41 ng/mL (normal <0.5)

[redacted] 20[redacted] PT: 17.6 SEC

[redacted] 20[redacted] PT: 11.1 SEC

[redacted] 20[redacted] RBC: 4.01 X10**6/MCL (normal 4.35 to 5.55)

[redacted] 20[redacted] RBC: 3.43 X10**6/MCL (normal 4.35 to 5.55)

[redacted] 20[redacted] SODIUM: 133 MMOL/L (normal 138 to 145)

[redacted] 20[redacted] SODIUM: 138 MMOL/L

[redacted] 20[redacted] TOTAL PROTEIN: 5.54 G/DL (normal 6.60 to 8.10)

[redacted] 20[redacted] TOTAL PROTEIN: 5.89 G/DL

[redacted] 20[redacted] WBC: 5.6 X10**3/MCL (normal 3.3 to 8.6)

[redacted] 20[redacted] WBC: 1.9 X10**3/MCL (normal 3.3 to 8.6)