Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[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悪化が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。腹痛を伴う血液が混じった下痢（1日当たり最大 11 回），食欲不振，貧血，白血球増加症，及び C 反応性たん白値の上昇を含む兆候及び症状が認められた。被験者の潰瘍性大腸炎の悪化症状は，ステロイド依存性及び免疫抑制剤不耐性患者を対象としたコルチコステロイド療法に対し，反応性が悪かった。20[redacted] 年 [redacted] 月 [redacted] 日，軟性 S 状結腸鏡検査が実施された結果，重度の疾患（特発性出血及び潰瘍形成）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，結腸切除術及び回腸瘻造設が実施され，合併症は認められなかった。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，被験者は退院した。

治療薬として Midanium（ミダゾラム），Ketalar（ケタミン塩酸塩），及びプロポフォールが投与された。

The patient's past medications include:

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

MECAPTOPURINUM VIS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

GRIPEX for COMMON COLD ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

---

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: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ULCERATIVE COLITIS AGGRAVATED

- Investigator: AGGRAVATION OF ULCERATIVE COLITIS AFTER CORTICOSTEROIDS WITHDRAWAL

- AbbVie: The event is exacerbation of underlying disease

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
ADALIMUMAB 40 MG EVERY WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: OVARIAN CYST RESECETION	19[redacted]
OTHER: RHINITIS, MOST PROBABLY OF ALLERGIC ORIGIN	20[redacted]
OTHER: POSTCORTICOSTEROIDAL HIRSUTISM	20[redacted]
OTHER: POSTSTEROID ACNE	20[redacted]
OTHER: HEADACHE	20[redacted]
OTHER: TRANSIENT NAUSEA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.05 PACKS	15	
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INTRAUTERINE CONTRACEPTIVE DEVICE	1 DEVICE	Other: PERMANENTLY	Y-M: 20[redacted]
PARACETAMOL	1000 mg (milligram(s))	PRN	Y-M: 20[redacted]
PREDNISONE	60 mg (milligram(s))	QD	Y-M: 20[redacted] / -267
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -259
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted] / -165
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -165
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -151
FORTRANS	148 g (gram(s))	QD	Y-M: 20[redacted] / -19
METAMIZOLE	500 mg (milligram(s))	QD	Y-M: 20[redacted] / -18
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -18
PROPOFOL	130 mg (milligram(s))	QD	Y-M: 20[redacted] / -18
IBUPROFEN	400 mg (milligram(s))	PRN	Y-M: 20[redacted] / -11

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
INTRAUTERINE CONTRACEPTIVE DEVICE	1 DEVICE	Other: PERMANENTLY	Y-M: 20[redacted]	ONGOING
PARACETAMOL	1000 mg (milligram(s))	PRN	Y-M: 20[redacted]	ONGOING
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted] / -165	ONGOING
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / 60	ONGOING
IRON	160 mg (milligram(s))	BID	Y-M: 20[redacted] / 138	Y-M: 20[redacted] / 355

CLOBETASOL	0.05 % (percent)	Other: EVERY OTHER DAY	Y-M: 20[redacted] / 144	ONGOING
THERAFLEX	1 DF (dosage form)	QD	Y-M: 20[redacted] / 281	ONGOING
BILASTINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 291	Y-M: 20[redacted] / 363
NIFUROXAZIDE	200 mg (milligram(s))	TID	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 338
FENTANYL	0.05 mcg (microgram(s))	QD	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 367
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 367
PROPOFOL	110 mg (milligram(s))	QD	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 367

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS AGGRAVATED
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 336
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 419): HEMATOCRIT: 0.36 [0.37 - 0.47] FRACTION; HEMOGLOBIN: 114 [120 - 160] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 21.4 [NOT REPORTED - 5] MG/L; WHITE BLOOD COUNT: 14.7 [4 - 10] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 421): Blood PCR -RT CMV: N

SAE Supplemental Procedure

(RX DAY): SIGMOIDOSCOPY: ACTIVE ULCERATIVE COLITIS; [redacted]20[redacted] (RX DAY 420): CHEST X-RAY: SMALL FOCUS OF INCREASED DENSITY IN THE APEX OF THE LEFT LUNG, MOST PROBABLY POSTINLFAMMATORY IN NATURE; ABDOMINAL ULTRASOUND: THICKENED WALL OF THE LEFT COLON - INFLAMMATORY LESIONS

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	CORTICOSTEROID DEPENDENT ULCERATIVE COLITIS; A NEW FLARE OD DISEASE AFTER CORTICOSTEROID THERAPY WITHDRAWAL
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[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悪化が認められた。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，潰瘍性大腸炎の悪化が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者はステロイド依存性の潰瘍性大腸炎患者であり，アダリムマブ治療に部分奏効しか示さなかったため，追加治療選択のために入院予定であった病院に搬送された。入院時に，血液が混じった下痢（1 日当たり最大 5 回）及び腹痛を含む症状が認められた。臨床検査及び内視鏡検査の結果，軽度から中等度の潰瘍性大腸炎の診断が確定された。インフリキシマブ導入療法が提示され，被験者は承諾した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
20[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 日の間に，非重篤な潰瘍性大腸炎の悪化が認められていた。

The patient's past medications include:

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

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

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

METYPRED 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], [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 40MG/0.8ML (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: No

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of ULCERATIVE COLITIS AGGRAVATED

- Investigator: Corticosteroid dependent ulcerative colits; a new flare OD disease after corticosteroid therapy withdrawal

- AbbVie: THE EVENT IS EXACERBATION OF UNDERLYING DISEASE OF UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL ULTRASOUND: thickened wall of the left colon - inflammatory lesions

[redacted] 20[redacted] CHEST X-RAY: Small focus of increased density in the apex of the left lung, most probably post inflammatory in nature

[redacted] 20[redacted] Colonoscopy:

- Rectum: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

- Sigmoid: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

- Descending colon: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

- Transverse colon: 1 = Mild disease (erythema, decreased vascular pattern, mild friability)

- Ascending colon/cecum: 0 = Normal or inactive disease

- Presence of friability: yes

- Subscore: 2

[redacted] 20[redacted] Flexible sigmoidoscopy:

- Rectum: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

- Sigmoid: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

- Presence of friability: Yes

- Subscore: 2

[redacted] 20[redacted] Flexible sigmoidoscopy:

- Rectum: 0 = Normal or inactive disease

- Sigmoid: 1 = Mild disease (erythema, decreased vascular pattern, mild friability)

- Descending colon: 0 = Normal or inactive disease

- Presence of friability: Yes

- Subscore: 1

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
アラニンアミノトランスフェラーゼ増加	X			
アスパラギン酸アミノトランスフェラーゼ増加	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK3[redacted]		FEMALE	White

Medical History	Onset Year
OTHER: AGENESIS OF THE LEFT KIDNEY	19[redacted]
OTHER: VESICOURTERAL REFLUX	19[redacted]
HYPERTHYROIDISM	19[redacted]
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	20[redacted]
OTHER: BREAST CYST 7 MM	20[redacted]
OTHER: OVARIAN CYST	20[redacted]
OTHER: SPONTANEOUS ABORTION	20[redacted]
DIABETES MELLITUS: DURING CORTICOSTEROID THERAPY	20[redacted]
OTHER: ASYMPTOMATIC ELEVATION OF TRANSAMINASES, PROBABLY DUE TO FORMER HBV INFECTION	20[redacted]
OTHER: CORTICOSTEROID-INDUCED ACNE	20[redacted]
OTHER: ABDOMINAL PAIN	20[redacted]
OTHER: UTERINE MYOMA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 51	51
ADALIMUMAB 4040 MG MG EVERY OTHER WEEK		EOW	[redacted]20[redacted] / 60	[redacted]20[redacted] / 256	197

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]
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted]
MERCAPTOPURINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -218
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -195
MESALAZINE	1500 mg (milligram(s))	BID	Y-M: 20[redacted] / -130
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -130
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / -18
FORTRANS	111 g (gram(s))	QD	Y-M: 20[redacted] / -15
ETOMIDATE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
PROPOFOL	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
SUFENTANIL	10 mcg (microgram(s))	QD	Y-M: 20[redacted] / -14
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -11

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
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -195	Y-M: 20[redacted] / 125
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / -18	ONGOING

CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 190
POTASSIUM	391 mg (milligram(s))	BID	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 190
FLUTICASONE	1 DF (dosage form)	BID	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 174
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted] / 18	Y-M: 20[redacted] / 155
CLOTRIMAZOLE	1 DF (dosage form)	BID	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 174
TERBINAFINE	1 DF (dosage form)	BID	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 94
ALFACALCIDOL	0.25 mcg (microgram(s))	QD	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 190
METHYLPREDNISOLONE	24 mg (milligram(s))	QD	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 92
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 89
METHYLPREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 106
CICLOPIROX	1 DF (dosage form)	BID	Y-M: 20[redacted] / 94	Y-M: 20[redacted] / 135
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] / 107	Y-M: 20[redacted] / 120
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 134
METHYLPREDNISOLONE	8 mg (milligram(s))	QD	Y-M: 20[redacted] / 135	Y-M: 20[redacted] / 148
TERBINAFINE	1 DF (dosage form)	BID	Y-M: 20[redacted] / 136	Y-M: 20[redacted] / 174

Event #1: Serious Adverse Event

Event Description	CLINICALLY SIGNIFICANT ALT ELEVATION, MILD AST ELEVATION
Preferred term	アラニンアミノトランスフェラーゼ増加，アスパラギン酸アミノトランスフェラーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 113
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 128): ALANINE AMINO TRANSFERASE (SGPT/ALT): 52 [0 - 35] U/L; ALBUMIN: 60.7 [52 - 65.1] %; ALKALINE PHOSPHATASE: 24 [30 - 120] U/L; ANTI-HBE ANTIBODY: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT PROVIDED; ANTI-HCV ANTIBOGY: NOT REACITVE [NOT REPORTED - NOT

REPORTED] NOT PROVIDED; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 23 [0 - 35] U/L; FT4: 23.37 [12.8 - 20.4] PMOL/L; GAMMA-GLUTAMYLTRANSP: 16 [0 - 38] U/L; HBE ANTIGEN: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT PROVIDED; HBS ANTIGEN: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT PROVIDED; HBV PCR: NEGATIVE <15IU/ML [0 - 15] IU/ML; HEMOGLOBIN: 129 [120 - 160] G/L; INR: 0.94 [0.8 - 1.2] RATIO; TOTAL BILIRUBIN: 9 [5 - 21] MCMOL/L; TOTAL PROTEIN: 63 [66 - 83] G/L; TSH: 1.77 [0.27 - 4.2] UIU/ML; WHITE BLOOD COUNT: 7.5 [4 - 10] X10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 128): ABDOMINAL ULTRASOUND: LIVER NOT ENLARGED WITH FEATURES OF STEATOSIS. NO OTHER ABNORMALITY FOUND.

AE Stopped Rx Day	148
Duration of AE	36 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	CONCOMITANT TREATMENT WITH MERCAPTOPURINE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の臨床的意義のあるアラニンアミノトランスフェラーゼ（以下「ALT」）値の上昇及び軽度のアスパラギン酸アミノトランスフェラーゼ（以下「AST」）値の上昇が認められた。関連する病歴は，左側潰瘍性大腸炎及び B 型肝炎ウイルス（以下「HBV」）感染であった。

20[redacted] 年 [redacted] 月 [redacted] 日，臨床的意義のある ALT 値の上昇及び軽度の AST 値の上昇が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，臨床的意義のある ALT 値の上昇及び軽度の AST 値の上昇は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はトランスアミナーゼ値上昇のため家庭医により病院に搬送及び入院し，詳細な診断が実施された。被験者は無症状であった。肝疾患に関する結論は得られなかった。ALT 値は 52 U/L（基準値：0～35），AST 値は 23 U/L（基準値：0～35）であった。その他の臨床検査値は全て基準範囲内であった。超音波検査の結果，脂肪肝は認められなかった。HBV 感染は PCR 検査により除外され，C 型肝炎ウイルス（以下「HCV」）抗体検査の結果は陰

性であった。HBV DNA 及び HCV 抗体の再検査が推奨され，結果は共に陰性であった。投与 24 週時の ALT 値は 18 U/L，AST 値は 21 U/L 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:

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

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

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

Causality for HUMIRA (Blinded)

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1) ALT increased (10001845) (Alanine aminotransferase increased (10001551)) [v.21.0] [10001845]

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) AST increased (10003544) (Aspartate aminotransferase increased (10003481)) [v.21.0] [10003544]

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 CLINICALLY SIGNIFICANT ALT ELEVATION, MILD AST ELEVATION

- Investigator: Concomitant treatment with mercaptopurine

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] abdominal ultrasound:

-The live was not enlarged with features of steatosis. No abnormality found.

Unknown date ALT: 18 U/L

(week 24)

[redacted] 20[redacted] Anti-HBe Antibody: negative

[redacted] 20[redacted] Anti-HCV antibody: Not Reactive

Unknown date AST: 21 U/L

(week 24)

[redacted] 20[redacted] HBe Antigen: Negative

[redacted] 20[redacted] HBs Antigen: Negative

[redacted] 20[redacted] HBV PCR: Negative <15 IU/mL

[redacted] 20[redacted] SGOT/ALT: 23 U/L (normal 0 to 35)

[redacted] 20[redacted] SGPT/ALT: 52 U/L (normal 0 to 35)

[redacted] 20[redacted] Total billirubin: 0.51 mg/dl

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
むちゃ飲み	X			
マロリー・ワイス症候群	X			
上部消化管出血	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	3[redacted]	MALE	White

Medical History	Onset Year
OTHER: RECCURENT THROAT INFLAMMATION	20[redacted]
ANEMIA: MICROCYTIC ANAEMIA REALTED TO ULCERATIVE COLITIS, HGB AROUND 12 G/DL	20[redacted]
OTHER: HEADACHE	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

ADALIMUMAB 40/40/160/40/160/40 MG TDM	EOW/EW/EW/EW/EW/EW	[redacted]20[redacted] / 59	[redacted]20[redacted] / 358	300

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	10 mg (milligram(s))	BID	Y-M: 20[redacted]
LEKOVIT CA	1250 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -299
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / -298
METHYLPREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -298
MESALAZINE	1.5 g (gram(s))	BID	Y-M: 20[redacted]-[redacted] / -199
AUGMENTIN	1000 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / -63
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / -29
ETOMIDATE	4 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -11
FENTANYL	0.05 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -11
FORTRANS	148 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / -11
KETAMINE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -11
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -11
PROPOFOL	120 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -11

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: 20[redacted]-[redacted] / 57	Y-M: 20[redacted]-[redacted] / 330
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / 64	ONGOING
NEO ANGIN	1 DF (dosage form)	PRN	Y-M: 20[redacted]-[redacted] / 231	Y-M: 20[redacted]-[redacted] / 246
CALGEL	1 DF (dosage form)	PRN	Y-M: 20[redacted]-[redacted] / 231	Y-M: 20[redacted]-[redacted] / 256
PANTOPRAZOLE	DATA NOT AVALAIBLE DATA NOT AVALAIBLE	Other: DATA NOT AVALAIBLE	Y-M: 20[redacted]-[redacted] / 264	Y-M: 20[redacted]-[redacted] / 265
PANTOPRAZOLE	DATA NOT AVALAIBLE DATA NOT AVALAIBLE	Other: DATA NOT AVALAIBLE	Y-M: 20[redacted]-[redacted] / 266	Y-M: 20[redacted]-[redacted] / 267
PARA-SELTZER	2 DF (dosage form)	PRN	Y-M: 20[redacted]-[redacted] / 267	Y-M: 20[redacted]-[redacted] / 273
ESOMEPRAZOLE	80 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 267	Y-M: 20[redacted]-[redacted] / 295

Event #1: Serious Adverse Event

Event Description	UPPER GASTROINTESTINAL BLEEDING AFTER BINGE DRINKING - MALLORY-WEISS SYNDROME
Preferred term	むちゃ飲み，マロリー・ワイス症候群，上部消化管出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 264
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 264): ALANINE AMINO TRANSFERASE (SGPT/ALT): 86 [5 - 41] U/L; ALKALINE PHOSPHATASE: 85 [40 - 129] U/L; AMYLASE: 115 [28 - 100] IU/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 98 [5 - 37] U/L; ETHANOL: 0.03 [0 - 0.05] G/L; HEMOGLOBIN: 124 [140 - 170] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 2.8 [NOT REPORTED - NOT REPORTED] MG/L; PLATELET COUNT: 418 [150 - 400] X10^9/L; TOTAL BILIRUBIN: 11 [5 - 21] MCMOL/L; WHITE BLOOD COUNT: 20.6 [4.5 - 10] X10^9/L; [redacted]20[redacted] (RX DAY 267): ALANINE AMINO TRANSFERASE (SGPT/ALT): 29 [5 - 41] U/L; AMYLASE: 75 [28 - 100] IU/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 15 [5 - 37] U/L; HEMOGLOBIN: 115 [140 - 170] G/L; PLATELET COUNT: 348 [150 - 400] X10^9/L; TOTAL BILIRUBIN: 21 [5 - 21] MCMOL/L; WHITE BLOOD COUNT: 10.4 [4.5 - 10] X10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 264): ABDOMINAL ULTRASOUND: NORMAL; ABDOMINAL X-RAY: NORMAL;
[redacted]20[redacted] (RX DAY 266): GASTROSCOPY: OESOPHAGITIS "B" IN LA SCALE, EROSIVE GASTRITIS.

AE Stopped Rx Day	267
Duration of AE	4 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	VOMITTING AFTER BINGE DRINKING
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象のむちゃ飲み後の上部消化管出血（マロリー・ワイス症候群）が認められた。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，むちゃ飲み後の上部消化管出血（マロリー・ワイス症候群）が認められた。20[redacted] 年[redacted] 月[redacted] 日，むちゃ飲み後の上部消化管出血（マロリー・ワイス症候群）は回復した。
20[redacted] 年[redacted] 月[redacted] 日，被験者は突然の吐血，並びに 3 ヵ月間続く咽喉痛及び嗄声のため入院した。被験者の状態は概ね良好であり，貧血はみられなかった。
治療薬としてパントプラゾール，Nolpaza，Apap Extra，及び Emanera が投与された。

The patient's past medications include:

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

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

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

AUGMENTIN for COMMON COLD ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Upper gastrointestinal bleeding (10071910) (Upper gastrointestinal haemorrhage (10046274)) [v.19.0] [10071910]

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

2) Binge drinking (10071238) (Binge drinking (10071238)) [v.19.0] [10071238]

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

3) Mallory-Weiss syndrome (10026712) (Mallory-Weiss syndrome (10026712)) [v.19.0] [10026712]

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 (Open Label)

Event of UPPER GASTROINTESTINAL BLEEDING AFTER BINGE DRINKING - MALLORY-WEISS SYNDROME

- Investigator: Vomiting after binge drinking

- AbbVie: Due to reported binge drinking

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Abdominal ultrasound: normal

[redacted] 20[redacted] Abdominal x-ray: normal

[redacted] 20[redacted] AMYLASE: 115 (normal 28 to 100)

[redacted] 20[redacted] ETHANOL: 0.03 G/L (normal <0.05)

[redacted] 20[redacted] Flexible Sigmoidoscopy:

[redacted] 20[redacted] Flexible Sigmoidoscopy:

[redacted] 20[redacted] Gastroscopy:

Rectum: 2 = Moderate diseasarked erythema, absent vascular pattern, friability, erosions); Sigmoid: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions); Descending colon: 1 = Mild disease (erythema, decreased vascular pattern, mild friability); Friability was present, Subscore = 2

[redacted] 20[redacted] HEMOGLOBIN: 11.5 G/DL (normal 14 to 17)

Rectum: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions); Sigmoid: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions); Friability was present, Subscore = 2

Esophagitis "B" in LA scale, erosive gastritis.

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 2.8

[redacted] 20[redacted] PLATELET COUNT: 418 X10**9/L (normal 150 to 400)

[redacted] 20[redacted] SGOT/AST: 15　(normal 5 to 37)

[redacted] 20[redacted] SGPT/ALT: 29 U/L (normal 5 to 41)

[redacted] 20[redacted] TOTAL BILIRUBIN: 1.22 mg/dL (normal 0.3 to 1.2)

[redacted] 20[redacted] WBC: 10.39 X10**9/L (normal 4.5 to 10)

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			
過剰皮膚	X			
体重減少	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	3[redacted]	MALE	White

Medical History	Onset Year
OBESITY	20[redacted]
OTHER: STRIAE ON THE SKIN OF THE ABDOMEN	20[redacted]
EYE DISEASE/DISORDER: CATARACT DUE TO CORTICOSTEROID THERAPY	20[redacted]
EYE DISEASE/DISORDER: CENTRAL RETINAL VEIN THROMBOSIS	20[redacted]
HYPERTENSION	20[redacted]
VALVULAR HEART DISEASE: TRICUSPID VALVE INSUFFICIENCY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 357	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MERCAPTOPURINE	50 mg (milligram(s))	QID	Y-M: 20[redacted]
MESALAZINE	1.5 g (gram(s))	BID	Y-M: 20[redacted]
MERCAPTOPURINE	50 mg (milligram(s))	TID	Y-M: 20[redacted]
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / -168
METHYLPREDNISOLONE	24 mg (milligram(s))	QD	Y-M: 20[redacted] / -39
FERRO-FOLSAN	1 DF (dosage form)	BID	Y-M: 20[redacted] / -35
METHYLPREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -27
INDAPAMIDE	1.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -26
PERINDOPRIL	8 mg (milligram(s))	QD	Y-M: 20[redacted] / -26
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] / -20
FORTRANS	4 SACHET	QD	Y-M: 20[redacted] / -16
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1.5 g (gram(s))	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 396
MERCAPTOPURINE	50 mg (milligram(s))	TID	Y-M: 20[redacted]	Y-M: 20[redacted] / 397
FERRO-FOLSAN	1 DF (dosage form)	BID	Y-M: 20[redacted] / 35	- Y-M: 20[redacted] / 396
INDAPAMIDE	1.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 26	- ONGOING
PERINDOPRIL	8 mg (milligram(s))	QD	Y-M: 20[redacted] / 26	- ONGOING
IRON	1 DF (dosage form)	QD	Y-M: 20[redacted] / 397	ONGOING
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / 397	ONGOING

MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / 398	ONGOING
ENOXAPARIN	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 398	Y-M: 20[redacted] / 406
METHYLPREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 399	Y-M: 20[redacted] / 402
CALCIUM CARBONATE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 401	Y-M: 20[redacted] / 406
METHYLPREDNISOLONE	60 mg (milligram(s))	Other: 40+20	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 406
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 405	Y-M: 20[redacted] / 418
LEKOVIT CA	1250 mg (milligram(s))	QD	Y-M: 20[redacted] / 406	ONGOING

Event #1: Serious Adverse Event

Event Description	SEVERE FLARE OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 366 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 397): ALBUMIN: 31 [35 - 52] G/L; HEMATOCRIT: 0.26 [0.42 - 0.52] FRACTION; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 44.6 [0 - 5] MG/L; PLATELET COUNT: 259 [148 - 400] X10^9/L; WHITE BLOOD COUNT: 1.3 [4 - 10] X10^9/L; [redacted]20[redacted] (RX DAY 402): ALBUMIN: 33 [35 - 52] G/L; [redacted]20[redacted] (RX DAY 405): HEMATOCRIT: 0.3 [0.42 - 0.52] FRACTION; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 68.5 [0 - 5] MG/L; PLATELET COUNT: 536 [148 - 400] X10^9/L; WHITE BLOOD COUNT: 4.1 [4 - 10] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 399): Stool CLOSTRIDIUM DIFFICILE TOXIN: N; [redacted]20[redacted] (RX DAY 400): Other SWAB, ULCERATIONS IN THE SCAR AEROBIC FLORA CULTURE: P-STAPHYLOCOCCUS AUREUS, ABUNDANT GROWTH; Blood PCR-REAL TIME CMV: N; [redacted]20[redacted] (RX DAY 401): Stool CULTURE OF FUNGI: N; [redacted]20[redacted] (RX DAY 402): Stool CULTURE: P-PROTEUS SPP ABUNDANT GROWTH; ENTEROCOCCUS FECIUM VRE - SINGLE COLONIES; [redacted]20[redacted] (RX DAY 405): Other SWAB, ULCERATIONS IN THE SCAR CULTURE OF ANAEROBIC FLORA: N; Other SWAB, ULCERATIONS IN THE SCAR CULTURE OF FUNGI: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 398): FLEXIBLE SIGMOIDOSCOPY: ACTIVE ULCERATIVE COLITIS, MAYO 3; [redacted]20[redacted] (RX DAY 399): CHEST X-RAY: NO SIGNIFICANT FINDINGS; ABDOMINAL ULTRASOUND: NO SIGNIFICANT FINDINGS

AE Stopped Rx Day	406 (49 DAYS AFTER LAST TREATMENT)
Duration of AE	41 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	DISCONTINUATION OF TREATMENT WITH STUDY DRUG

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

Event #2: Serious Adverse Event

Event Description	EXCESSIVE AND REDUNDANT SKIN FOLLOWING WEIGHT LOSS
Preferred term	過剰皮膚，体重減少
AE Onset Date / Rx Day	[redacted]20[redacted] / 370 (13 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 370): ABDOMINOPLASTY: SURGERY WITHOUT COMPLICATIONS.

AE Stopped Rx Day	372 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	OBESITY IN PATIENT'S HISTORY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の体重減少に続く過剰皮膚及びたるみが認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，体重減少に続く過剰皮膚及びたるみが認められた。20[redacted] 年 [redacted] 月 [redacted] 日，体重減少に続く過剰皮膚及びたるみは回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。以前に著しく肥満体であった被験者は，栄養士の管理下で 30 kg を超える体重を減量した。体重減少により，腹部に皮膚線条を伴う過剰皮膚が発現し，整形手術による治療の適応となった。20[redacted] 年 [redacted] 月 [redacted] 日，腹壁形成術が実施され，合併症は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Excessive skin (10064503) (Excessive skin (10064503)) [v.22.0] [10064503]

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) Weight loss (10047900) (Weight decreased (10047895)) [v.22.0] [10047900]

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 EXCESSIVE AND REDUNDANT SKIN FOLLOWING WEIGHT LOSS

- Investigator: Obesity in patient's history.

- AbbVie: The patient has known pre-existing obesity and lost over 30 kg under a dietician's care.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の重度の潰瘍性大腸炎再燃が認められた。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，重度の潰瘍性大腸炎再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，重度の潰瘍性大腸炎再燃は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，約 1 ヵ月前に発現した潰瘍性大腸炎の悪化のため，被験者は入院した。入院の際に，被験者から血液が混じった軟便（毎日，1 日当たり最大 8 回），腹痛，及び体温上昇の報告があった。身体的診察の結果，下腹部の疼痛，及び腹壁形成術後の瘢痕に黄色の膿が滲出した 3 つの潰瘍形成が認められた。臨床検査の結果，汎血球減少症，低アルブミン血症，鉄欠乏症，及び C 反応性たん白値の上昇が認められた。本事象に関連するリスク因子は，治験薬投与の中止であった。本事象は以前にも認められていた（20[redacted] 年 [redacted] 月）。本事象に対する一連の治療として，メチルプレドニゾロン，エノキサパリン，シプロフロキサシン，及び栄養補助剤の静脈内投与が開始された。メルカプトプリンの投与は中止された。被験者の容体は改善し，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。
治療薬として Pentasa（メサラジン），Calperos，Cipronex（シプロフロキサシン），メルカプトプリン，Metypred（メチルプレドニゾロンコハク酸エステルナトリウム），Protifar，Vitrum Calcium＋ビタミン D3，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），Clexane（エノキサパリンナトリウム），Tardyferon，シプロフロキサシン，エノキサパリン，メチルプレドニゾロン，及び Asamax（メサラジン）が投与された。

Causality for HUMIRA 40MG/0.8ML (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 40MG/0.8ML (Open Label)

Event of SEVERE FLARE OF ULCERATIVE COLITIS

- Investigator: Discontinuation of treatment with study drug.

- AbbVie: The event is exacerbation of underlying UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL ULTRASOUND: No significant findings

[redacted] 20[redacted] AEROBIC FLORA CULTURE (SWAB, ULCERATIONS IN THE SCAR): Positive: staphylococcus aureus,abundant growth

[redacted] 20[redacted] ALBUMIN: 31 G/L (normal 35 to 52)

[redacted] 20[redacted] ALBUMIN: 33 G/L (normal 35 to 52)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 44.6 MG/L (normal 0 to 5)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 68.5 MG/L (normal 0 to 5)

[redacted] 20[redacted] CHEST X-RAY: No significant findings

[redacted] 20[redacted] CLOSTRIDIUM DIFFICILE TOXIN: Stool: Negative

[redacted] 20[redacted] CULTURE OF ANAEROBIC FLORA (SWAB, ULCERATIONS IN THE SCAR): Negative

[redacted] 20[redacted] CULTURE OF FUNGI (SWAB, ULCERATIONS IN THE SCAR): Negative

[redacted] 20[redacted] FLEXIBLE SIGMOIDOSCOPY: Active ulcerative colitis, Mayo 3

[redacted] 20[redacted] HEMATOCRIT: 26.2 % (normal 42.0 to 52.0)

[redacted] 20[redacted] HEMATOCRIT: 30.1 % (normal 42.0 to 52.0)

[redacted] 20[redacted] NEUTROPHILS: 1.01 X10**9/L (normal 3 to 5.8)

[redacted] 20[redacted] NEUTROPHILS: 1.53 X10**9/L (normal 3 to 5.8)

[redacted] 20[redacted] PCR - REAL TIME CMV: Blood: Negative

[redacted] 20[redacted] STOOL CULTURE: Positive: Proteus spp abundant growth; enterococcus fecium VRE - single colonies

[redacted] 20[redacted] STOOL CULTURE OF FUNGI: 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
肺炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	3[redacted]	MALE	White

Medical History	Onset Year
OTHER: FISTULA CONNECTING THROAT WITH RIGHT EXTERNAL EAR	19[redacted]
OTHER: DRY COUGH WITH NO OTHER SYMPTOMS AND SIGNS AND NO FINDINGS ON CHEST X-RAY, ACCOMPANYING THE EXACERABTIONS OF ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 4040 MG MG EVERY WEEK		EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 359	303

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]
INFLIXIMAB	5 mg/kg (milligram(s)/kilogram)	Other: 0-2-6 WEEK	Y-M: 20[redacted]
AZATHIOPRINE	75 mg (milligram(s))	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -157
MESALAZINE	1.5 g (gram(s))	BID	Y-M: 20[redacted] / -97
LOPERAMIDE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / -32
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -31
FORTRANS	148 g (gram(s))	QD	Y-M: 20[redacted] / -19

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	75 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 140
MESALAZINE	1.5 g (gram(s))	BID	Y-M: 20[redacted] / -97	ONGOING
PHLEBODRIL	1 DF (dosage form)	BID	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 111
PREDNISONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 102	Y-M: 20[redacted] / 108
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 115
PREDNISONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 122
PARACETAMOL	1 DF (dosage form)	PRN	Y-M: 20[redacted] / 138	Y-M: 20[redacted] / 144
CEFTRIAXONE	2 g (gram(s))	QD	Y-M: 20[redacted] / 138	Y-M: 20[redacted] / 150
CLARITHROMYCIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 138	Y-M: 20[redacted] / 150

Event #1: Serious Adverse Event

Event Description	RIGHT-SIDED PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 138
Age at AE Onset	3[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 138): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 126.2 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY

144): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 25.6 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 142): Sputum MYCOBACTERIUM TUBERCULOSIS COMPLEX PCR: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 138): CHEST X-RAY: DENSE CONSOLIDATION CONFINED TO THE LOWER LOBE OF THE RIGHT LUNG CORRESPONDING TO INFLAMMATORY LESIONS. SMALL AMOUNT OF FLUID IN THE RIGHT PLEURAL CAVITY.; [redacted]20[redacted] (RX DAY 143): CHEST X-RAY: INFLAMMATORY CONSOLIDATION CONFINED TO THE LOWER LOBE OF THE RIGHT LUNG AND THE TRACE OF FLUID IN THE RIGHT PLEURAL CAVITY.; [redacted]20[redacted] (RX DAY 150): CHEST X-RAY: INFLAMMATORY CONSOLIDATION CONFINED TO THE LOWER LOBE OF THE RIGHT LUNG AND THE TRACE OF FLUID IN THE RIGHT PLEURAL CAVITY.; [redacted]20[redacted] (RX DAY 211): CHEST X-RAY: PERIBRONCHIAL WIDENING AND PARENCHYMAL REACTION CONFINED TO THE LOWER LOBE OF THE RIGHT LUNG AND THE TRACE OF FLUID IN THE RIGHT PLEURAL CAVITY - SMALLER THAN ON THE PREVIOUS SCAN.

AE Stopped Rx Day	246
Duration of AE	109 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の右肺炎が認められた。関連する病歴は，左側潰瘍性大腸炎，潰瘍性大腸炎の悪化を伴うが他の兆候・症状及び胸部 X 線検査における所見を伴わない乾性咳嗽であった。

20[redacted] 年 [redacted] 月 [redacted] 日，右肺炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，右肺炎は回復した。

入院の 3 週間前に，気道感染の症状が発現した。症状が悪化したため，20[redacted] 年 [redacted] 月 [redacted] 日に現地の病院に入院した。抗生剤投与による治療が行われ，良好な治療効果が得られた。重篤な有害事象である本事象に関連した兆候及び症状は，発熱，咳嗽，及び呼吸困難であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者は，本事象に関連するリスク因子又は家族歴を有していなかった。

治療薬としてアセトアミノフェン，Klacid（クラリスロマイシン），及び Biotrakson が投与された。

The patient's past medications include:

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

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

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.20.0] [10035664]

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: rechallenge was done, outcome unknown

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of RIGHT-SIDED PNEUMONIA

- Investigator: Not applicable.

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CHEST X-RAY: dense consolidation confined to the lower lobe of the right lung corresponding to inflammatory lesions. small amount of fluid n the right pleural cavity.

[redacted] 20[redacted] CHEST X-RAY: Inflammatory consolidation confined to the lower lobe of the right lung and the trace of the fluid in the right pleural cavity.

[redacted] 20[redacted] CHEST X-RAY: Inflammatory consolidation confined to the lower lobe of the right lung and the trace of the fluid in the right pleural cavity.

[redacted] 20[redacted] CHEST X-RAY: Peribronchial widening and Parenchymal reaction CONFINED TO THE LOWER LOBE OF THE RIGHT LUNG AND THE TRACE OF FLUID IN THE RIGHT PLEURAL CAVITY - smaller than on the previous scan.

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 126.2 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 25.6 MG/L

[redacted] 20[redacted] SPUTUM CULTURE: Mycobacterium tuberculosis complex PCR- 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
ADALIMUMAB 40 MG EVERY WEEK	5[redacted]	MALE	White

Medical History	Onset Year
OBESITY	19[redacted]
OTHER: SPINAL FRACTURE	20[redacted]
PERIPHERAL VASCULAR DISEASE-VENOUS: THROMBOPHLEBITIS	20[redacted]
EYE DISEASE/DISORDER: SENILE VISION DEFECT	20[redacted]
OSTEOARTHRITIS	20[redacted]
OTHER: GASTRIC EROSIONS	20[redacted]
OTHER: MACROCYTIC ANAEMIA	20[redacted]
OTHER: PRURIGO NODULARIS	20[redacted]
HYPERLIPIDEMIA: HYPERCHOLESTOROLAEMIA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	12	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted]
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted]
INFLIXIMAB	470 mg (milligram(s))	Other: 0-2-6 WEEK	Y-M: 20[redacted]
ALFACALCIDOL	1 mcg (microgram(s))	QD	Y-M: 20[redacted] / -180
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] / -126
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -74
POTASSIUM	2 DF (dosage form)	QD	Y-M: 20[redacted] / -74
CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / -59
VITAMIN B COMPLEX	500 mcg (microgram(s))	QD	Y-M: 20[redacted] / -59
FORTRANS	2 SACHET	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
SULFASALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted]	Y-M: 20[redacted] / 388
ALFACALCIDOL	1 mcg (microgram(s))	QD	Y-M: 20[redacted] / -180	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -74	ONGOING
POTASSIUM	2 DF (dosage form)	QD	Y-M: 20[redacted] / -74	ONGOING
CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / -59	ONGOING
VITAMIN B COMPLEX	500 mcg (microgram(s))	QD	Y-M: 20[redacted] / -59	ONGOING

DYNAMAG	1 DF (dosage form)	QD	Y-M: 20[redacted] / 114	ONGOING
IRON	1 DF (dosage form)	QD	Y-M: 20[redacted] / 156	ONGOING
METHYLPREDNISOLONE	24 mg (milligram(s))	QD	Y-M: 20[redacted] / 353	Y-M: 20[redacted] / 388
SOLUTIONS FOR PARENTERAL NUTRITION	NOT REPORTED	Other: UKNOWN	Y-M: 20[redacted] / 389	Y-M: 20[redacted] / 406
STEROIDS	NOT REPORTED	Other: UNKNOWN	Y-M: 20[redacted] / 389	Y-M: 20[redacted] / 406
FOLIC ACID	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 406	ONGOING
POTASSIUM	1 TABLET	TID	Y-M: 20[redacted] / 406	ONGOING
SULFASALAZINE	2 mg (milligram(s))	BID	Y-M: 20[redacted] / 406	ONGOING
METHYLPREDNISOLONE	48 mg (milligram(s))	QD	Y-M: 20[redacted] / 406	Y-M: 20[redacted] / 412

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS AGGRAVATED
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 389 (31 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	406 (48 DAYS AFTER LAST TREATMENT)
Duration of AE	18 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ULCERATIVE COLITIS AGGRAVATED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（ポーランド）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，肥満，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］），及び胃粘膜びらんであった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 12 年）であり，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。被験者の症状はさらに悪化し，連日の腹痛を伴う血液が混じった軟便（1 日当たり 15 回）がみられた。コルチコステロイドの静脈内投与及び高カロリー輸液による治療が実施された。被験者に臨床的改善がみられ始めた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Sulfasalazinum（サラゾスルファピリジン），Metypred（メチルプレドニゾロンコハク酸エステルナトリウム），及び非経口ステロイドの投与，並びに高カロリー輸液が実施された。

Causality for HUMIRA 40MG/0.8ML (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: Not Applicable

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

Event of ULCERATIVE COLITIS AGGRAVATED

- Investigator: ULCERATIVE COLITIS AGGRAVATED

- AbbVie: EVENT 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
鼻茸	X			
副鼻腔ポリープ	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	MALE	White

Medical History	Onset Year
SURGERY: SURGERY OF THE NASAL SEPTUM AND REMOVAL OF POLYPS	20[redacted]
SURGERY: SURGERY TO REMOVE THE APPENDIX	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.02 PACKS	2	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / -352
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -260
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -163
FORTRANS	74 g (gram(s))	QID	Y-M: 20[redacted] / -13
LOPERAMIDE	2 mg (milligram(s))	BID	Y-M: 20[redacted] / -4

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / -352	ONGOING
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -163	ONGOING
CEFUROXIME	1.5 g (gram(s))	BID	Y-M: 20[redacted] / 353	Y-M: 20[redacted] / 355
DEXKETOPROFEN	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 353	Y-M: 20[redacted] / 355
PARACETAMOL	UNK UNK	Other: UNK	Y-M: 20[redacted] / 353	Y-M: 20[redacted] / 355
CALCIUM	100 mg (milligram(s))	TID	Y-M: 20[redacted] / 355	ONGOING
OXYMETAZOLINE	UNK UNK	TID	Y-M: 20[redacted] / 355	Y-M: 20[redacted] / 357
CIRRUS	125 mg (milligram(s))	BID	Y-M: 20[redacted] / 355	Y-M: 20[redacted] / 358
CEFUROXIME	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 355	Y-M: 20[redacted] / 360

Event #1: Serious Adverse Event

Event Description	RECURRENT NASAL AND PARANASAL SINUSES POLYPS
Preferred term	鼻茸，副鼻腔ポリープ
AE Onset Date / Rx Day	[redacted]20[redacted] / 353
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 353): GLUCOSE: 5.4 [4.1 - 5.5] MMOL/L; HEMATOCRIT: 0.41 [0.4 - 0.55] FRACTION; HEMOGLOBIN: 150 [140 - 180] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 3 [0 - 60] MG/L; PLATELET COUNT: 232 [150 - 400] X10^9/L; POTASSIUM: 4.6 [3.5 - 5.1] MMOL/L; RED BLOOD COUNT: 4.7 [4.2 - 6.1] X10^12/L; SODIUM: 141 [136 - 146] MMOL/L; WHITE BLOOD COUNT: 6.4 [4 - 11] X10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 353): BILATERAL REPOLIPECTOMY AND ETHMOIDECTOM: POLYPS IN NOSE WAS REMOVED

AE Stopped Rx Day	355
Duration of AE	3 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	POLYPS IN THE NOSE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，20[redacted] 年 [redacted] 月 [redacted] 日に重篤な有害事象の鼻及び副鼻腔ポリープの再発が認められた。関連する病歴は，鼻中隔手術及びポリープ切除であった。
20[redacted] 年 [redacted] 月 [redacted] 日，鼻及び副鼻腔ポリープの再発が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，鼻及び副鼻腔ポリープは回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，ポリープにより鼻呼吸が困難となり，被験者は入院した。被験者は鼻茸の既往歴を有しており，鼻及び副鼻腔ポリープの再発が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，両側ポリープ再切除術及び内視鏡下篩骨洞手術が実施され，鼻のポリープが除去された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な容体で退院した。
治療薬として Bioracef，Nasivin soft（オキシメタゾリン塩酸塩），カルシウム，Cirrus，Pronasal（Mometasoni furoas），Dexak，Biofuroksym，及び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) Nasal polyp (10028754) (Nasal polyps (10028756)) [v.20.0] [10028754]

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)　Sinus polyp (10040749)　(Sinus polyp (10040749))　[v.20.0]　[10040749]

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 RECURRENT NASAL AND PARANASAL SINUSES POLYPS

- Investigator: Polyps in the nose.

- AbbVie: The event is related to pre-existing condition.

Event of RECURRENT NASAL AND PARANASAL SINUSES POLYPS

- Investigator: Polyps in the nose.

- AbbVie: The event is related to pre-existing condition.

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			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	4[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: WOUND CUT BACK LEFT FOOT RIDGE- LEFT BIG TOE INJURY - SURGERY RECONSTRUCTION	20[redacted]
VENOUS THROMBOEMBOLISM: THROMBOPHLEBITIS	20[redacted]
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

ADALIMUMAB 40/40/160/40/160/40 MG TDM	EOW/EW/EW/EW/EW/EW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 357	300

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -153
FOLIC ACID	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -148
PANTOPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -148
PREDNISONE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -89
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -58
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -20
FORTRANS	296 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
FOLIC ACID	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -148	ONGOING
PANTOPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -148	ONGOING
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -58	ONGOING
DEXAMETHASONE	2 gtt (drop(s))	BID	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 114
TROXERUTIN	2 gtt (drop(s))	BID	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 114
SPEKTRAMOX	1 TABLET 875MG+ 125MG	TID	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 134
PANTOPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 134	ONGOING
IRON	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 134
CEFUROXIME	1.5 g (gram(s))	BID	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 142
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 147
COLECALCIFEROL	15000 IU (international unit(s))	QD	Y-M: 20[redacted] / 142	ONGOING

Event #1: Serious Adverse Event

Event Description	ERYTHEMA NODOSUM
Preferred term	結節性紅斑
AE Onset Date / Rx Day	[redacted]20[redacted] / 134
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 134): CREATININE: 60 [44 - 80] MCMOL/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 145 [0 - 5] MG/L; IRON: 10 [33 - 193] MCG/DL; POTASSIUM: 4.4 [3.5 - 5.1] MMOL/L; SODIUM: 134 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 135): VITAMIN D: 6 [30 - 80] NG/ML; [redacted]20[redacted] (RX DAY 142): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 180 [0 - 50] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 134): CHEST X-RAY: NO SIGNIFICANT CHANGES

AE Stopped Rx Day	142
Duration of AE	9 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UNKNOWN.POSSIBLE RELATIONSHIP WITH STUDY DISEASE OR UPPER RESPIRATORY INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の結節性紅斑が認められた。20[redacted] 年[redacted] 月[redacted] 日，結節性紅斑が認められた。20[redacted] 年[redacted] 月[redacted] 日，結節性紅斑は回復した。

本事象の発現前である 20[redacted] 年[redacted] 月[redacted] 日には，呼吸器感染が認められている。20[redacted] 年[redacted] 月[redacted] 日，被験者は広範囲の腫脹を伴う前脛部の発疹及び頻脈のため入院した。被験者は結節性紅斑と診断された。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。

治療薬として Biofuroksym が投与された。

The patient's past medications include:

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

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1)　Erythema nodosum (10015226)　(Erythema nodosum (10015226))　[v.21.1]　[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 40MG/0.8ML (Blinded)

Event of ERYTHEMA NODOSUM

- Investigator: Unknown. Possible relationship with study disease or upper respiratory infection.

- AbbVie: Risk factors include the preceding respiratory infection and pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CREATININE: 0.68 mg/dL (normal 0.5 to 0.9)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 145 MG/L (normal 0.0 to 5.0)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 18 mg/dL (normal 0.0 to 5.0)

[redacted] 20[redacted] IRON: 10 UG/DL (normal 33 to 193)

[redacted] 20[redacted] LYMPHOCYTES: 1.22 THOUS/UL (normal 1.18 to 3.74)

[redacted] 20[redacted] POTASSIUM: 4.4 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] SODIUM: 134 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] VITAMIN D: 6 NG/ML (normal 30 to 80)

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			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	MALE	White

Medical History	Onset Year
ANEMIA: SECONDARY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 4040 MG MG EVERY OTHER WEEK		EOW	[redacted]20[redacted] / 64	[redacted]20[redacted] / 358	295

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FERRO-FOLSAN	1 TABLET	BID	Y-M: 20[redacted]
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	8 mg (milligram(s))	BID	Y-M: 20[redacted] / -200
FORTRANS	4 SACHETS	QD	Y-M: 20[redacted] / -22
FENTANYL	0,1 mg (milligram(s))	QD	Y-M: 20[redacted] / -21
MIDAZOLAM	2 mg (milligram(s))	QD	Y-M: 20[redacted] / -21
PROPOFOL	80 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
FERRO-FOLSAN	1 TABLET	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 424
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted]	Y-M: 20[redacted] / 424
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 424
METHYLPREDNISOLONE	16 mg (milligram(s))	BID	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 424
IRON	UNK		Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 232
IRON	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / 345	Y-M: 20[redacted] / 345
RED BLOOD CELLS	2 DF (dosage form)	Other: ONCE	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 429
AKRITOIN	100 mg (milligram(s))	BID	Y-M: 20[redacted] / 432	ONGOING
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] / 434	ONGOING
OMEPRAZOLE	20 mg (milligram(s))	PRN	Y-M: 20[redacted] / 434	ONGOING
ULTRACET	1 TABLET	PRN	Y-M: 20[redacted] / 434	ONGOING

Event #1: Serious Adverse Event

Event Description	SECONDARY ANEMIA INCREASING
Preferred term	貧血

AE Onset Date / Rx Day	[redacted]20[redacted] / 225
Age at AE Onset	31

Laboratory Testing

[redacted]20[redacted] (RX DAY 225): HEMATOCRIT: 0.28 [0.39 - 0.5] FRACTION; HEMOGLOBIN: 85 [135 - 175] G/L; [redacted]20[redacted] (RX DAY 228): ALANINE AMINO TRANSFERASE (SGPT/ALT): 8 [10 - 41] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 16 [10 - 50] U/L; BUN: 10.4 [6.8 - 15.7] MMOL/L; CREATININE: 71 [44 - 106] MCMOL/L; GLUCOSE: 5.6 [3.9 - 5.5] MMOL/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 567 [0 - 50] MG/L; POTASSIUM: 4 [3.5 - 5.1] MMOL/L; SODIUM: 139 [136 - 145] MMOL/L; TOTAL BILIRUBIN: 2 [3 - 17] MCMOL/L; TOTAL PROTEIN: 68 [63 - 83] G/L; URIC ACID: 250 [214 - 488] MCMOL/L; URINE PH: 5 [4.8 - 7.4] N/A; URINE PROTEIN (DIPSTICK TEST): 52.1 [0 - 12] MG/DL; URINE SPECIFIC GRAVITY: 1020 [1016 - 1026] N/A; [redacted]20[redacted] (RX DAY 231): HEMATOCRIT: 0.3 [0.39 - 0.5] FRACTION; HEMOGLOBIN: 88 [135 - 175] G/L; PLATELET COUNT: 548 [150 - 450] X10^9/L; RED BLOOD COUNT: 4 [4.3 - 5.7] X10^12/L; RETICULOCYTES: 1.17 [0.48 - 1.64] %; WHITE BLOOD COUNT: 3.6 [4 - 10.5] X10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 228): ECG: IN NORMAL RANGE (IRBB IS NCS)

AE Stopped Rx Day	232
Duration of AE	8 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	SYMPTOMATIC SECONDARY ANEMIA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	SECONDARY ANEMIA INCREASE
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 335
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 344): ALANINE AMINO TRANSFERASE (SGPT/ALT): 6 [5 - 35] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 9 [7 - 40] U/L; CREATININE: 77 [80 - 115] MCMOL/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 46.3 [NOT REPORTED - NOT REPORTED] MG/L; POTASSIUM: 4.4 [3.5 - 4.5] MMOL/L; SODIUM: 135 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 345): FERRUM: 10 [NOT REPORTED - NOT REPORTED] UG/DL; HEMATOCRIT: 0.25 [0.39 - 0.49] FRACTION; HEMOGLOBIN: 73 [132 - 173] G/L; MCV: 71.9 [NOT REPORTED - NOT REPORTED] FL; PLATELET COUNT: 811 [NOT REPORTED - NOT REPORTED] G/L; RED BLOOD COUNT: 3.5 [4.3 - 5.7] X10^12/L; WHITE BLOOD COUNT: 4.2 [NOT REPORTED - NOT REPORTED] G/L; [redacted]20[redacted] (RX DAY 346): FERRITIN LEVEL: 124 [NOT REPORTED - NOT REPORTED] NG/ML

Microbiology

NOT REPORTED

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	SECONDARY ANEMIA DUE TO ULCETATIVE COLITIS MUCOSAL BLEEDING
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 424 (66 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 424): HEMOGLOBIN: 115 [132 - 173] G/L; PLATELET COUNT: 686 [NOT REPORTED - NOT REPORTED] G/L; WHITE BLOOD COUNT: 8.68 [NOT REPORTED - NOT REPORTED] G/L; [redacted]20[redacted] (RX DAY 428): HEMOGLOBIN: 89 [132 - 173] G/L; [redacted]20[redacted] (RX DAY 429): WHITE BLOOD COUNT: 11.16 [NOT REPORTED - NOT REPORTED] G/L; [redacted]20[redacted] (RX DAY 433): HEMOGLOBIN: 102 [132 - 173] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 18.2 [NOT REPORTED - NOT REPORTED] MG/L; PLATELET COUNT: 463 [NOT REPORTED - NOT REPORTED] G/L; WHITE BLOOD COUNT: 4.97 [NOT REPORTED - NOT REPORTED] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 424): CHEST X-RAY: NORMAL; [redacted]20[redacted] (RX DAY 427): TOTAL PROCTOCOLECTOMY WITH ILEOANAL J-PO: SURGERY; [redacted]20[redacted] (RX DAY 432): UROLOGY CONSULTATION: DYSURIA - FARMACOLOGY TREATMET PRESCRIBED

AE Stopped Rx Day	427 (69 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	PANCOLECTOMY DUE TO FLARE OF COLITIS WITHOUT RESPONSE FOR STEROID, IMMUNOSUPRESANTS AND ANTYTNF TREATMENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の二次性貧血の増加が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，二次性貧血の増加が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，二次性貧血の増加は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，症候性二次性貧血が認められ，被験者は入院した。本事象に関連する兆候及び症状は，臨床検査結果におけるヘモグロビン値の減少であった。20[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 日にかけて，Ferrum（フマル酸第一鉄）の静脈内投与による治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Ferinject（カルボキシマルトース第二鉄）が投与された。

The patient's past medications include:

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

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

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

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

CIPRONEX for ULCERATIVE COLITIS and URINARY INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Secondary anemia (10054606) (Anaemia (10002034)) [v.18.1] [10054606]

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 (Open Label)

Event of SECONDARY ANEMIA INCREASING

- Investigator: SYMPTOMATIC SECONDARY ANEMIA

- AbbVie: THE EVENT IS EXACERBATION OF PREEXISTING ANEMIA PRIOR TO THE STUDY ENTRY.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Hematocrit: 28.4 % (normal >38.8 to <50.0)

[redacted] 20[redacted] Hematocrit: 30.4 % (normal >38.8 to <50.0)

[redacted] 20[redacted] Hemoglobin: 8.5 G/DL (normal >13.5 to <17.5)

[redacted] 20[redacted] Hemoglobin: 8.8 G/DL (normal >13.5 to <17.5)

[redacted] 20[redacted] RBC: 3.99 (normal >4.32 to <5.72)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の二次性貧血の増加が認められた。関連する病歴は，左側潰瘍性大腸炎及び二次性貧血であった。
20[redacted] 年 [redacted] 月 [redacted] 日，二次性貧血の増加が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，ヘモグロビン値の減少を伴う症候性二次性貧血が認められ，被験者はFerrum（フマル酸第一鉄）の静脈内投与による治療のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Monover が投与された。

The patient's past medications include:

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

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

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

PACKED RED BLOOD CELLS for SECONDARY ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

CIPRONEX for ULCERATIVE COLITIS and URINARY INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Anemia aggravated (10054309) (Anaemia (10002034)) [v.19.0] [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

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of SECONDARY ANEMIA INCREASE

- Investigator: Secondary anemia due to ulcerative colitis mucosal bleeding.

- AbbVie: The event is exacerbation of pre-existing anemia prior to the study entry.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Hematocrit: 25.1 %

[redacted] 20[redacted] Hemoglobin: 7.3 G/DL

[redacted] 20[redacted] Platelet count: 811 G/L
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎再燃が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，ステロイド剤，免疫抑制剤，及び他の抗 TNF 治療に奏効を示さない大腸炎再燃が認められたため，結腸全摘術が行われ，J 型回腸嚢肛門吻合及び一時的回腸人工肛門造設術が実施された。血が混じった下痢，貧血の再発，脱力，及び生活の質の低下を含む兆候及び症状が認められた。また，赤血球濃厚液投与による治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃は回復した。
治療薬として Furaginum，Poltram Combo，及び Polprazol（オメプラゾール）が投与された。

The patient's past medications include:

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

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

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

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.1] [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 40MG/0.8ML (Open Label)

Event of ULCERATIVE COLITIS FLARE

- Investigator: PANCOLECTOMY due to flare of colitis without response for steroid, immunosuppressants and any TNF treatment

- AbbVie: The event is exacerbation of underlying UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

- severe disease (spontaneous bleeding, ulceration in rectum, sigmoid and descending colon; transverse colon and ascending colon/cecum were normal or inactive disease.

[redacted] 20[redacted] Flexible sigmoidoscopy:

- severe disease (spontaneous bleeding, ulceration) in rectum and sigmoid.

[redacted] 20[redacted] Flexible sigmoidoscopy:

- severe disease (spontaneous bleeding, ulceration) in rectum and sigmoid.

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
上腕骨骨折	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	4[redacted]	MALE	White

Medical History	Onset Year
HYPERTENSION	20[redacted]
ANEMIA: SECONDARY ANEMIA	20[redacted]
OTHER: SECONDARY THROMBOCYTHEMIA	20[redacted]
SURGERY: SURGERY TREATMENT OF FRACTURE LEFT HUMERUS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	10	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 361	305

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	200 mg (milligram(s))	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	8 mg (milligram(s))	QD	Y-M: 20[redacted]
RAMIPRIL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted]
MERCAPTOPURINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -186
MESALAZINE	60 mL (millilitre(s))	QD	Y-M: 20[redacted] / -32
FORTRANS	4 SACHETS	Other: ONCE	Y-M: 20[redacted] / -11
FENTANYL	0.1 mg (milligram(s))	QD	Y-M: 20[redacted] / -10
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -10
PROPOFOL	200 mg (milligram(s))	QD	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
RAMIPRIL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted]	ONGOING
HYDROXYZINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 164
MODAFINIL	10 mg (milligram(s))	PRN	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 164
CLARITHROMYCIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 154
CEFTRIAXONE	UNK mg (milligram(s))		Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 179
NADROPARIN	UNK mg (milligram(s))	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 179
OMEPRAZOLE	UNK mg (milligram(s))		Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 179
TRAMADOL	UNK mg (milligram(s))		Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 179
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 180	ONGOING
PHLEBODRIL	1 TABLET	TID	Y-M: 20[redacted] / 180	ONGOING
ULTRACET	1 TABLET	PRN	Y-M: 20[redacted] / 180	ONGOING

FERRO-FOLSAN	1 TABLET	BID	Y-M: 20[redacted] / 206	Y-M: 20[redacted] / 260
CEFAZOLIN	1 AMPULES	Other: UNKNOWN	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 312
METAMIZOLE	1 AMPULES	PRN	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 312
PANTOPRAZOLE	1 TABLET	QD	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 312
PARACETAMOL	1 AMPULES	PRN	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 312
TRAMADOL	1 TABLET	PRN	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 312

Event #1: Serious Adverse Event

Event Description	FRACTURE OF THE RIGHT HUMERUS
Preferred term	上腕骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 163
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 174): SURGERY TREATMENT FRACTURE OF THE RIGHT:

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HOSPITALISATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	FRACTURE OF THE LEFT HUMERUS
Preferred term	上腕骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 301
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 305): SURGERY TREATMENT: RESOLVING

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HOSPITALISATION WITH SURGERY TREATMENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の右上腕骨骨折が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型），高血圧，二次性貧血，二次性血小板血症，及び左上腕骨骨折の外科治療であった。被験者は元喫煙者（1 日当たり 0.5 箱，喫煙期間 10 年）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，右上腕骨骨折が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は凍結した歩道で転倒し，右上腕骨を骨折した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は外科治療のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，右上腕骨骨折の手術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Polprazol（オメプラゾール），Zaldiar effervescence，Cyclo 3 Fort，Biotrakson，Tardyferon Fol，及び Fraxiparine が投与された。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Humerus fracture (10020462) (Humerus fracture (10020462)) [v.22.0] [10020462]

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 FRACTURE OF THE RIGHT HUMERUS

- Investigator: Hospitalization.

- AbbVie: Likely related to a trauma.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の左上腕骨骨折が認められた。関連する病歴は，潰瘍性大腸炎（全大腸炎型），左上腕骨骨折の外科治療，及び右上腕骨骨折の外科治療であった。被験者は元喫煙者（1 日当たり 0.5 箱，喫煙期間 10 年）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，左上腕骨骨折が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左上腕骨骨折の外科治療のため入院した。被験者は自宅の階段から転落した。治験責任医師により，被験者は長期間にわたりステロイド治療を受けており，骨粗鬆症の高リスク因子を有していたと判断された。20[redacted] 年 [redacted] 月 [redacted] 日，手術が行われ，被験者は回復に向かった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者は以前に右上腕骨を骨折していた。

治療薬として Pyralgin，アセトアミノフェン，セファゾリン，IPP，及び Poltram が投与された。

The patient's past medications include:

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

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

METYPRED 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])

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

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

FORTRANS for BOWEL PREPARTION FOR COLONOSCOPY and BOWEL PREPARTION FOR COLONOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted])

FENTANYL for SEDATION DURING COLONOSCOPY and SEDATION DURING COLONOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted])

MIDANIUM for SEDATION DURING COLONOSCOPY and SEDATION DURING COLONOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted])

PROPOFOL for SEDATION DURING COLONOSCOPY and SEDATION DURING COLONOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted])

ATARAX for ITCHY SKIN ([redacted] 20[redacted] - [redacted] 20[redacted])

ALERTEC for SKIN RASH ([redacted] 20[redacted] - [redacted] 20[redacted])

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

BIOTRAKSON for FRACTURE OF THE RIGHT HUMERUS ([redacted] 20[redacted] - [redacted] 20[redacted])

FRAXIPARINE for FRACTURE OF THE RIGHT HUMERUS ([redacted] 20[redacted] - [redacted] 20[redacted])

HELICID for FRACTURE OF THE RIGHT HUMERUS ([redacted] 20[redacted] - [redacted] 20[redacted])

TRAMAL for FRACTURE OF THE RIGHT HUMERUS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1)　Humerus fracture (10020462)　(Humerus fracture (10020462))　[v.20.0]　[10020462]

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 FRACTURE OF THE LEFT HUMERUS

- Investigator: Hospitalization with surgery treatment.

- AbbVie: The event was due to a fall down the stairs in the patient's home.

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
眼瞼下垂	X	X		
感覚鈍麻	X	X		
単ニューロパチー	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	3[redacted]	MALE	White

Medical History	Onset Year
SURGERY: CHOLECYSTECTOMY	20[redacted]
OTHER: CHRONIC GASTRITIS	20[redacted]
ANEMIA: SECONDARY ANEMIA	20[redacted]
OTHER: LIVER HEMANGIOMAS	20[redacted]
OTHER: RIGHT KIDNEY CYST	20[redacted]
OTHER: THROMBOSIS OF THE SUPERFICIAL VEINS OF THE UPPER RIGHT EXTREMITY	20[redacted]
OTHER: PLEURAL FIBROSIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	6	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 344	288

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]-[redacted]
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -49
HYDROCORTISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -49
FERRO-FOLSAN	1 TABLET	BID	Y-M: 20[redacted]-[redacted] / -20
PREDNISONE	20 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -20
FORTRANS	4 SACHETS	QD	Y-M: 20[redacted]-[redacted] / -11
FENTANYL	0.1 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -10
MIDAZOLAM	2 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -10
PROPOFOL	260 mg (milligram(s))	QD	Y-M: 20[redacted]-[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
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted]-[redacted]	ONGOING
FERRO-FOLSAN	1 TABLET	BID	Y-M: 20[redacted]-[redacted] / -20	Y-M: 20[redacted]-[redacted] / 365
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 292	Y-M: 20[redacted]-[redacted] / 364
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 365	ONGOING
MUPIROCIN	1 DF (dosage form)	PRN	Y-M: 20[redacted]-[redacted] / 365	ONGOING
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 365	ONGOING

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

Event Description	ISOLATED ,IDIOPATIC MONONEUROPATHY IN THE REGION OF THE UPPER EYELID MUSCLE, RIGHT PTOSIS, HYPOAESTHESIA OF THE RIGHT EYEBROW
Preferred term	眼瞼下垂，感覚鈍麻，単ニューロパチー
AE Onset Date / Rx Day	[redacted]20[redacted] / 348 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 349): ALANINE AMINO TRANSFERASE (SGPT/ALT): 53 [0 - 41] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 23 [0 - 21] U/L; CHOLESTEROL: 4.55 [2.97 - 4.91] MMOL/L; CREATININE: 90 [62 - 106] MCMOL/L; GLUCOSE: 4.9 [4.1 - 5.9] MMOL/L; HDL CHOLESTEROL: 59.2 [40 - NOT REPORTED] MG/DL; HEMATOCRIT: 0.47 [0.38 - 0.54] FRACTION; HEMOGLOBIN: 159 [140 - 180] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 9.9 [0 - 5] MG/L; LDL CHOLESTEROL: 2.43 [0 - 2.97] MMOL/L; PLATELET COUNT: 226 [150 - 350] X10^9/L; POTASSIUM: 4.1 [3.5 - 5.1] MMOL/L; RED BLOOD COUNT: 5.5 [4.5 - 5.9] X10^12/L; SODIUM: 147 [136 - 145] MMOL/L; TOTAL BILIRUBIN: 8 [0 - 21] MCMOL/L; TRIGLYCERIDES: 1.31 [0 - 1.7] MMOL/L; TSH: 0.41 [0.27 - 4.2] IU/ML; URINE PH: SOUR [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; URINE SPECIFIC GRAVITY: 1027 [1015 - 1020] N/A; WHITE BLOOD COUNT: 7.4 [4 - 10] X10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 350): MAGNETIC RESONANCE OF THE BRAIN AND BRAI: WITHOUT ABNORMALITIES; ANGIO-MR CEREBRAL ARTERIES: WITHOUT ABNORMALITIES; OPHTHALMOLOGY CONSULTATION: HYPERTENSION ANGIOPATHY , ASTIGMATISM; CHEST X-RAY: WITHOUT ABNORMALITIES; MR OF EYE SOCKETS: WITHOUT ABNORMALITIES; [redacted]20[redacted] (RX DAY 351): ELECTROMYOGRAPHY: WITHOUT ABNORMALITIES; [redacted]20[redacted] (RX DAY 352): TRANSCRANIAL USG-DOPPLER OF CEREBRAL ART: WITHOUT ABNORMALITIES; USG-DOPPLER OF CEREBRAL AND VERTEBRAL AR: WITHOUT ABNORMALITIES

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	MAIN REASON WAS NOT UNRAVEL DURING HOSPITALISATION. ACCORDING TO NEUROLOGYST OPINION IT COULD BE IN RELATIONSHIP TO STUDY DRUG. IP WAS WITHDRAWN.EW VIST SCHEDULED ON [redacted]20[redacted].ISSUE NOT RESOLVED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の上眼瞼挙筋領域の孤立性かつ突発性単ニューロパチー，右眼瞼下垂，及び右眉の感覚鈍麻が認められた。関連する病歴は，左側潰瘍性大腸炎，貧血，及び右側上肢の浅静脈血栓症であった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 6 年）であり，アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，上眼瞼挙筋領域の孤立性かつ突発性単ニューロパチー，右眼瞼下垂，及び右眉の感覚鈍麻が認められた。

本事象の発現前には，20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日までの間に，非重篤な右眼瞼下垂が認められていた。

20[redacted] 年 [redacted] 月 [redacted] 日，眼瞼下垂，縮瞳，及び瞳孔不同症が認められ，被験者は入院した。直近に発症した疾患及び外傷，並びに新たな投薬はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，眼科を受診した際に，被験者は非重篤な高血圧性血管障害及び乱視と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院したが，本事象は回復しなかった。入院中に本事象の原因は確定されなかった。ホルネル症候群とは確定されなかった。

Causality for HUMIRA (Blinded)

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1) Mononeuropathy (10062203) (Mononeuropathy (10062203)) [v.21.1] [10062203]

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

2) Ptosis (10037272) (Eyelid ptosis (10015995)) [v.21.1] [10037272]

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

3) Localised numbness (10024775) (Hypoaesthesia (10020937)) [v.21.1] [10024775]

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

Alternative Etiology for HUMIRA (Blinded)

Event of ISOLATED, IDIOPATIC MONONEUROPATHY IN THE REGION OF THE UPPER EYELID MUSCLE

- Investigator: Not applicable

- AbbVie: Not applicable

Event of RIGHT PTOSIS

- Investigator: Not applicable

- AbbVie: Not applicable

Event of HYPOAESTHESIA OF THE RIGHT EYEBROW

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ANGIO-MR CEREBRAL ARTERIES: without abnormalities

[redacted] 20[redacted] BLOOD GLUCOSE: 4.9 MMOL/L (normal 4.11 to 5.89)

[redacted] 20[redacted] CHEST X-RAY: without abnormalities

[redacted] 20[redacted] CHOLESTEROL: 176 mg/dL (normal 115 to 190)

[redacted] 20[redacted] CREATININE: 90.3 MCMOL/L (normal 62.0 to 106.0)

[redacted] 20[redacted] ELECTROMYOGRAPHY: without abnormalities

[redacted] 20[redacted] HDL CHOLESTEROL: 59.2 mg/dL (normal >40)

[redacted] 20[redacted] HEMATOCRIT: 47.1 % (normal 38.0 to 54.0)

[redacted] 20[redacted] HEMOGLOBIN: 15.9 G/DL (normal 14.0 to 18.0)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 9.9 MG/L (normal 0.0 to 5.0)

[redacted] 20[redacted] LDL CHOLESTEROL: 94.1 mg/dL (normal 0.0 to 115)

[redacted] 20[redacted] MAGNETIC RESONANCE OF THE BRAIN AND BRAINSTEM: without abnormalities

[redacted] 20[redacted] MR OF EYE SOCKETS: without abnormalities

[redacted] 20[redacted] OPHTHALMOLOGY CONSULTATION: Hypertension angiopathy, astigmatism

[redacted] 20[redacted] PLATELET COUNT: 226 X10**9/L (normal 150 to 350)

[redacted] 20[redacted] POTASSIUM: 4.11 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] RBC: 5.53 X10**12/L (normal 4.5 to 5.9)

[redacted] 20[redacted] SGOT/AST: 22.8 U/L (normal 0.0 to 21.0)

[redacted] 20[redacted] SGPT/ALT: 52.5 U/L (normal 0.0 to 41.0)

[redacted] 20[redacted] SODIUM: 146.7 MMOL/L (normal 136.0 to 145.0)

[redacted] 20[redacted] TOTAL BILIRUBIN: 8.0 MCMOL/L (normal 0.0 to 21.0)

[redacted] 20[redacted] TRANSCRANIAL USG-DOPPLER OF CEREBRAL ARTERIES: without abnormalities

[redacted] 20[redacted] TRIGLYCERIDES: 116 mg/dL (normal 0 to 150)

[redacted] 20[redacted] TSH: 0.410 IU/mL (normal 0.270 to 4.200)

[redacted] 20[redacted] URINE PH: Sour

[redacted] 20[redacted] URINE SPECIFIC GRAVITY: 1027 no units (normal 1015 to 1020)

[redacted] 20[redacted] USG-DOPPLER OF CERVICAL AND VERTEBRAL ARTERIES: without abnormalities

[redacted] 20[redacted] WBC: 7.35 X10**9/L (normal 4.0 to 10.0)

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
潰瘍性大腸炎	X			
肺炎	X		X	

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	5[redacted]	MALE	White

Medical History	Onset Year
OTHER: CHRONIC GASTRITIS	20[redacted]
ANEMIA: SECONDARY ANEMIA	20[redacted]
DEPRESSION: MILD	20[redacted]
OTHER: STOMACH PAIN DUE TO UC	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44

ADALIMUMAB 40 MG 40 MG EVERY WEEK	EW	[redacted]20[redacted] / 58[redacted]20[redacted] / 183		126

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -270
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / -270
MERCAPTOPURINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -164
SWISS-KAL EFF	2 SACHETS	QD	Y-M: 20[redacted] / -164
TIANEPTINE	12,5 mg (milligram(s))	TID	Y-M: 20[redacted] / -164
ULTRACET	1 TABLET	PRN	Y-M: 20[redacted] / -73
FERRO-FOLSAN	1 TABLET	BID	Y-M: 20[redacted] / -15
PICO-SALAX	4 SACHETS	QD	Y-M: 20[redacted] / -13
FENTANYL	0.1 mg (milligram(s))	QD	Y-M: 20[redacted] / -12
PROPOFOL	180 mg (milligram(s))	QD	Y-M: 20[redacted] / -12
INFLUENZA VACCINE	1 DF (dosage form)	QD	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / -270	Y-M: 20[redacted] / 199
TIANEPTINE	12,5 mg (milligram(s))	TID	Y-M: 20[redacted] / -164	Y-M: 20[redacted] / 184
SWISS-KAL EFF	2 SACHETS	QD	Y-M: 20[redacted] / -164	Y-M: 20[redacted] / 202
ULTRACET	1 TABLET	PRN	Y-M: 20[redacted] / -73	Y-M: 20[redacted] / 185
FERRO-FOLSAN	1 TABLET	BID	Y-M: 20[redacted] / -15	Y-M: 20[redacted] / 185
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 183
ALBUMIN HUMAN	UNKNOWN L (litre(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
CARBOHYDRATES NOS W/LIPIDS NOS/MINE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201

ENOXAPARIN	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
GLUCOSE	UNKNOWN L (litre(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
IRON	700 mg (milligram(s))	QD	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
MESALAZINE	1000 mg (milligram(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
PANTOPRAZOLE	40 mg (milligram(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
PARACETAMOL	1 g (gram(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
POTASSIUM	1 CAPSULE	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
POTASSIUM	UNKNOWN mEq (milliequivalent(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
RIFAXIMIN	200 mg (milligram(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
SODIUM CHLORIDE	UNK L (litre(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
SPIRONOLACTONE	100 mg (milligram(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
SPIRONOLACTONE	200 mg (milligram(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
SPIRONOLACTONE	25 mg (milligram(s))	Other: UNNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
TRAMADOL	1 AMPULE	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
TRAMADOL	100 mg (milligram(s))	Other: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 185
HYDROCORTISONE	100 mg (milligram(s))	QID	Y-M: 20[redacted] / 185	Y-M: 20[redacted] / 196
SERTRALINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 199
PREDNISONE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 202
SPIRONOLACTONE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 202
ULTRACET	1 TABLET	TID	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 202

INFLIXIMAB	300 mg (milligram(s))	QD	Y-M: 20[redacted] / 198 Y-M: 20[redacted] / 198
DEXLANSOPRAZOLE	30 mg (milligram(s))	BID	Y-M: 20[redacted] / 198 Y-M: 20[redacted] / 199
DROTAVERINE	80 mg (milligram(s))	TID	Y-M: 20[redacted] / 198 Y-M: 20[redacted] / 199
FERRO-FOLSAN	1 TABLET	TID	Y-M: 20[redacted] / 198 Y-M: 20[redacted] / 199
AUGMENTIN	UNK mg (milligram(s))	Other: UNKNOWN	Y-M: 20[redacted] / 199 Y-M: 20[redacted] / 200
BROMHEXINE	1 TABLET	BID	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
CEFUROXIME	1.5 g (gram(s))	TID	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
CIPROFLOXACIN	400 mg (milligram(s))	BID	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
DUOVENT	1 DF (dosage form)	BID	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
ELECTROLYTE SOLUTIONS	0.5 L (litre(s))	BID	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
ENOXAPARIN	60 mg (milligram(s))	QD	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
FUROSEMIDE	1 AMPULE	BID	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
HYDROCORTISONE	100 mg (milligram(s))	PRN	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
MAGNESIUM SULFATE	1 AMPULE	QD	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
METOPROLOL	2.5 mg (milligram(s))	BID	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
MORPHINE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202
THEOPHYLLINE	1 DF (dosage form)	QD	Y-M: 20[redacted] / 200 Y-M: 20[redacted] / 202

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS WORSENING
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 185 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 185): HEMOGLOBIN: 127 [131 - 172] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 60 [NOT REPORTED - NOT REPORTED] MG/DL; WHITE BLOOD COUNT: 10.7 [NOT REPORTED - NOT REPORTED] G/L; [redacted]20[redacted] (RX DAY 186): GDH: NEGATIVE [NOT REPORTED - NOT REPORTED] UNKNOWN; [redacted]20[redacted] (RX DAY 189): QUANTIFERON TB: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; [redacted]20[redacted] (RX DAY 192): ALBUMIN: 31 [34 - 48] G/L; [redacted]20[redacted] (RX DAY 196): HEMOGLOBIN: 12 [131 - 172] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 52.1 [NOT REPORTED - NOT REPORTED] MG/DL; WHITE BLOOD COUNT: 16.4 [NOT REPORTED - NOT REPORTED] G/L

Microbiology

[redacted]20[redacted] (RX DAY 186): Stool PATOLOGICAL VIRAL CULTURE: P-ADENOVIRUS ANTYGEN DETECTION; Stool PATOLOGICAL FUNGAL CULTURE: N; Stool PATOLOGICAL BACTERIOLOGICAL CULTURE: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 185): ABDOMEN USG: ABNORMAL- NCS; ABDOMEN X-RAY: ABNORMAL /NCS/; [redacted]20[redacted] (RX DAY 186): UROLOGICAL CONSULTATION: ABNORMAL - NCS; [redacted]20[redacted] (RX DAY 189): ECG: NORMAL; CHEST X-RAY: NORMAL

AE Stopped Rx Day	196 (13 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	PATIENT WAS WITHDRAWN FROM STUDY DUE TO PRIMARY NO RESPONSE FOR ADALIMUUMAB TREATMENT AND DIRECTED TO HOSPITALISATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event, Death

Event Description	PNEUMONIA WORSENING
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 200 (17 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 200): PROCALCYTONIN: 1.6 [NOT REPORTED - NOT REPORTED] NG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 204): AUTOPSY RAPORT: PULMONARY EMBOLISM, EDEMA OF THE BRAIN, ASPERGILLOSIS OF THE LUNGS AND BRONCHI

AE Stopped Rx Day	202 (19 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS

Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	INFORMATION WILL BE UPDATED WHEN AVAILABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING, DEATH OF SUBJECT

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（ポーランド）であり，重篤な有害事象で致死性の肺炎の悪化及び潰瘍性大腸炎の悪化が認められた。関連する病歴は，慢性胃炎，左側潰瘍性大腸炎，二次性貧血，軽度のうつ病，及び潰瘍性大腸炎による胃痛であった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 20 年）であり，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，肺炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死亡原因は肺炎の悪化，肺アスペルギルス症，肺塞栓症，及び脳浮腫として報告された。検死解剖により，肺炎の悪化，肺アスペルギルス症，及び肺塞栓症が確定された。

20[redacted] 年 [redacted] 月 [redacted] 日，ステロイド剤又はアダリムマブによる外来治療に奏効を示さない活動性の潰瘍性大腸炎が認められ，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。アダリムマブ治療において奏効がみられなかったため，被験者は試験を中止した。被験者は潰瘍性大腸炎再燃による入院歴を有していた。

20[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 日の間に非重篤な肺炎が認められていた。

入院前に被験者は肺炎と診断された。抗生剤による治療効果は得られなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎の悪化のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。検死解剖結果が報告された。主な死亡原因は肺塞栓症であった。また，脳浮腫及び肺気管支アスペルギルス症が原因として報告された。

治療薬として Natrium chloratum，Poltram，Glucosum 5%，Aldactone（スピロノラクトン），Xifaxan（リファキシミン），Flexbumin，Protifar，Clexane（エノキサパリンナトリウム），Glucosum 10%，アセトアミノフェン，Kalium chloratum 15%，Kaldyum，Zaldiar，Verospiron（スピロノラクトン），インフリキシマブ，NO-SPA Forte，Amoksiklav，Cipronex（シプロフロキサ

シン），モルヒネ塩酸塩，Metocard（メトプロロール酒石酸塩），Furosemidum（フロセミド），Biofuroxim，電解質液，Berodual，Flegaminum，Corhydrone，Theophyllaminum，Tramal（トラマドール塩酸塩），Spironol，Pentasa（メサラジン），Nolpaza，ヒドロコルチゾン，及び硫酸マグネシウムが投与された。

The patient's past medications include:

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

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

INFLUVAC for VACCINATION AGAINST INFLUENZA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Pneumonia aggravated (10048382) (Pneumonia (10035664)) [v.21.0] [10048382]

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.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: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of PNEUMONIA WORSENING

- Investigator: Not Reported.

- AbbVie: Event is likely a nosocomial infection. Risk factors include recent hospitalization for worsening ulcerative colitis and stool testing positive for adenovirus.

Event of ULCERATIVE COLITIS WORSENING

- Investigator: Patient was withdrawn from study due to primary no response for adalimumab treatment and directed to hospitalization.

- AbbVie: Recurring flare of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL USG: Normal/NCS

[redacted] 20[redacted] ABDOMINAL X-RAY: Abnormal/NCS

[redacted] 20[redacted] ALBUMIN: 3.05 G/DL

[redacted] 20[redacted] BLOOD QUANTIFERON TB: Negative

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

[redacted] 20[redacted] ECG: Normal

[redacted] 20[redacted] HEMOGLOBIN: 12.7 G/DL

[redacted] 20[redacted] HEMOGLOBIN: 11.5 G/L

[redacted] 20[redacted] HIGH SENSITIVITY C-REACTIVE PROTEIN: 60 mg/dL

[redacted] 20[redacted] HIGH SENSITIVITY C-REACTIVE PROTEIN: 52.1 mg/dL

[redacted] 20[redacted] PATHOLOGICAL FUNGAL CULTURE STOOL: Negative

[redacted] 20[redacted] PATHOLOGICAL FUNGAL CULTURE STOOL: Negative

[redacted] 20[redacted] PATHOLOGICAL VIRAL CULTURE STOOL: adenovirus antigen detection

[redacted] 20[redacted] PROCALCYTONIN: 1.6 ng/mL

[redacted] 20[redacted] STOOL GDH: Negative

[redacted] 20[redacted] UROLOGICAL CONSULTATION: Abnormal/NCS

[redacted] 20[redacted] WBC: 10.7 G/L

[redacted] 20[redacted] WBC: 16.4 G/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
穿孔性十二指腸潰瘍	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	MALE	White

Medical History	Onset Year
ANEMIA: SECONDARY ANEMIA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -289
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -154
SULFASALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -154
MESALAZINE	60 mL (millilitre(s))	QD	Y-M: 20[redacted] / -140
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -57
PICO-SALAX	2 SACHETS	QD	Y-M: 20[redacted] / -15
ATROPINE	0,5 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
FENTANYL	0.1 mcg (microgram(s))	QD	Y-M: 20[redacted] / -14
PROPOFOL	200 mg (milligram(s))	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
SULFASALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -154	ONGOING
PANTOPRAZOLE	1 AMUPLE	QD	Y-M: 20[redacted] / 227	Y-M: 20[redacted] / 261
SODIUM CHLORIDE	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 227	Y-M: 20[redacted] / 261
DROTAVERINE	1 AMPULE	QD	Y-M: 20[redacted] / 227	Y-M: 20[redacted] / 287
HYOSCINE	1 DF (dosage form)	QD	Y-M: 20[redacted] / 227	Y-M: 20[redacted] / 287
METAMIZOLE	1 AMPULE	QD	Y-M: 20[redacted] / 227	Y-M: 20[redacted] / 287
METOCLOPRAMIDE	1 AMPULE	QD	Y-M: 20[redacted] / 227	Y-M: 20[redacted] / 287
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 254
OMEPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 261	ONGOING
OMEPRAZOLE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / 261	Y-M: 20[redacted] / 261
ULTRACET	1 TABLET	PRN	Y-M: 20[redacted] / 261	Y-M: 20[redacted] / 275

Event #1: Serious Adverse Event

Event Description	ULCER OF THE DUODENUM BULB WITH PERFORATION
Preferred term	穿孔性十二指腸潰瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 252
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 253): CREATININE: 74 [62 - 115] MCMOL/L; HEMOGLOBIN: 150 [140 - 180] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 1.95 [NOT REPORTED - 5] MG/L; LIPASE: 24 [12 - 53] U/L; WHITE BLOOD COUNT: 19.3 [4 - 10] X10^9/L; [redacted]20[redacted] (RX DAY 255): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 255.12 [NOT REPORTED - 5] MG/L; PLATELET COUNT: 243 [150 - 450] X10^9/L; POTASSIUM: 3.3 [3.5 - 5.5] MMOL/L; PROCALCITONIN: 0.2 [NOT REPORTED - 0.5] NG/ML; SODIUM: 137 [132 - 146] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 254): GASTROSCOPY: GERD, EROSIVE GASTRITIS AND DUODENITIS; [redacted]20[redacted] (RX DAY 255): ABDOMEN AND PELVIS CT: SUSPICION OF GASTROINTESTINAL PERFORATION; SURGICAL TREATMENT OF DUODENAL PERFORATI: EFFECTIVE

AE Stopped Rx Day	261
Duration of AE	10 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	PATIENT WAS HOSPITALISED FOR DIAGNOSTIC SEVERE ABDOMINAL PAIN. ABDOMEN CT RESULT :SUSPICION OF GI PERFORATION. DURING DIAGNOSTIC LAPAROTOMY PERFORATION OF DUODENAL BULB WAS CONFIRMED AND RESOLVED.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の穿孔を伴う十二指腸球部潰瘍が認められた。関連する病歴は，二次性貧血，潰瘍性大腸炎（全大腸炎型），及び大腸内視鏡検査であった。被験者は非喫煙者であり，アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，穿孔を伴う十二指腸球部潰瘍が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，穿孔を伴う十二指腸球部潰瘍は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は重度の腹痛の診断検査のため入院した。コンピュータ断層撮影検査が実施され，消化管穿孔の疑いが認められた。20[redacted] 年 [redacted] 月 [redacted] 日，開腹術が実施され，十二指腸球部の穿孔部の治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。被験者は本事象に関連するリスク因子（潰瘍性大腸炎の悪化）を有していた。被験者は本事象に関連する家族歴を有していなかった。また，本事象の既往歴もなかった。

治療薬として Metoclopramidum（メトクロプラミド），Palgotal，IPP，Natrium chloratum，Pyralginu，NO-SPA，Glucosum 5% fresenius，及び Helicid Forte（オメプラゾール）が投与された。

The patient's past medications include:

CORTIMENT MMX 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])

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

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Ulcer duodenal with perforation (10045301) (Duodenal ulcer perforation (10013849)) [v.21.0] [10045301]

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 40MG/0.8ML (Blinded)

Event of ULCER OF THE DUODENUM BULB WITH PERFORATION

- Investigator:

- AbbVie: Event more likely related to chronic therapy with sulfasalazine.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] SODIUM: 136.9 MMOL/L (normal 132.0 to 146.0)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 1.95 MG/L (normal <= 5.0)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 255.12 MG/L (normal <= 5.0)

Unknown date COMPUTED TOMOGRAPHY: suspicion of gastrointestinal (GI) perforation

[redacted] 20[redacted] CREATININE: 74.32 MCMOL/L (normal 61.9 to 114.9)

[redacted] 20[redacted] GASTROSCOPY: GERD, Erosive gastritis and duodenitis

[redacted] 20[redacted] HEMOGLOBIN: 150 G/L(normal 140.0 to 180.0)

[redacted] 20[redacted] LIPASE: 24 U/L (normal 12 to 53)

[redacted] 20[redacted] PLATELET COUNT: 243.0 X10**9/L (normal 150.0 to 450.0)

[redacted] 20[redacted] POTASSIUM: 3.3 MMOL/L (normal 3.5 to 5.5)

[redacted] 20[redacted] PROCALCITONIN: 0.2 NG/ML (normal <= 0.5)

[redacted] 20[redacted] WBC: 19.26 X10**9/L (normal 4.0 to 10.0)

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
関節痛	X			
高血圧	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	4[redacted]	MALE	White

Medical History	Onset Year
HYPERTENSION	20[redacted]
OTHER: NONALCOHOLIC FATTY LIVER DISEASE-NAFLD	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: NON EROSIVE REFLUX DISEASE	20[redacted]
OTHER: COLON INFLAMMATORY POLYPS	20[redacted]
OTHER: RIGHT HAND FINGERS INJURY	20[redacted]
PERIPHERAL NERVE DISORDER: PERIPHERAL FACIAL NERVE PALSY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 357	300

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AMLODIPINE	10 mg (milligram(s))	QD	Y-M: 20[redacted]
NEBIVOLOL	5 mg (milligram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -249
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / -249
METHYLPREDNISOLONE	48 mg (milligram(s))	QD	Y-M: 20[redacted] / -157
AZATHIOPRINE	200 mg (milligram(s))	QD	Y-M: 20[redacted] / -146
HYDROCORTISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -146
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -146
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -79
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / -79
PANTOPRAZOLE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / -79
BUTYRIC ACID	150 mg (milligram(s))	BID	Y-M: 20[redacted] / -41
METHYLPREDNISOLONE	24 mg (milligram(s))	QD	Y-M: 20[redacted] / -41
PROBIOTICS	1 CAPSULE	QD	Y-M: 20[redacted] / -41
CLINDAMYCIN	300 mg (milligram(s))	TID	Y-M: 20[redacted] / -27
AUGMENTIN	1 g (gram(s))	BID	Y-M: 20[redacted] / -21
FORTRANS	1 SACHET	QID	Y-M: 20[redacted] / -14
FENTANYL	0,1 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
PROPOFOL	260 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
AMLODIPINE	10 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 149

NEBIVOLOL	5 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 149
AZATHIOPRINE	200 mg (milligram(s))	QD	Y-M: 20[redacted]	/ONGOING -146
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted]	/ONGOING -146
PANTOPRAZOLE	20 mg (milligram(s))	BID	Y-M: 20[redacted]	/ONGOING -79
POTASSIUM	1 CAPSULE	BID	Y-M: 20[redacted]	/Y-M: 20[redacted] / 6 420
ACICLOVIR	800 mg (milligram(s))	Other: EVERY 6 HOURS	Y-M: 20[redacted]	/Y-M: 20[redacted] / 70 149
ULTRACET	1 TABLET	PRN	Y-M: 20[redacted]	/Y-M: 20[redacted] / 96 124
FUROSEMIDE	1 AMPULE	BID	Y-M: 20[redacted]	/Y-M: 20[redacted] / 149 154
RAMIPRIL	5 mg (milligram(s))	BID	Y-M: 20[redacted]	/Y-M: 20[redacted] / 150 163
TORASEMIDE	5 mg (milligram(s))	QD	Y-M: 20[redacted]	/Y-M: 20[redacted] / 150 163
METHYLPREDNISOLONE	8 mg (milligram(s))	QD	Y-M: 20[redacted]	/Y-M: 20[redacted] / 150 165
NEBIVOLOL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]	/Y-M: 20[redacted] / 150 420
CYANOCOBALAMIN	1000 mcg (microgram(s))	QD	Y-M: 20[redacted]	/Y-M: 20[redacted] / 154 158
CANDESARTAN	16 mg (milligram(s))	QD	Y-M: 20[redacted]	/Y-M: 20[redacted] / 164 420
MILRINONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]	/Y-M: 20[redacted] / 164 420
METHYLPREDNISOLONE	4 mg (milligram(s))	QD	Y-M: 20[redacted]	/ONGOING 166
CLINDAMYCIN	300 mg (milligram(s))	TID	Y-M: 20[redacted]	/Y-M: 20[redacted] / 249 252
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted]	/ONGOING 363
FUROSEMIDE	1 AMPULE	Other: UNKNOWN	Y-M: 20[redacted]	/Y-M: 20[redacted] / 420 426
POTASSIUM	3 g (gram(s))	Other: UNKNOWN	Y-M: 20[redacted]	/Y-M: 20[redacted] / 420 426
SODIUM CHLORIDE	100 mL (millilitre(s))	Other: UNKNOWN	Y-M: 20[redacted]	/Y-M: 20[redacted] / 420 426

SODIUM CHLORIDE	500 mL (millilitre(s))	Other: UNKNOWN	Y-M: 20[redacted] /Y-M: 20[redacted] / 420 426
URAPIDIL	1 AMPULE	Other: UNKNOWN	Y-M: 20[redacted] /Y-M: 20[redacted] / 420 426
AMLODIPINE BESILATE W/INDAPAMIDE/PE	1 TABLET	QD	Y-M: 20[redacted] /ONGOING 426
HYDROXYZINE	45 mg (milligram(s))	QD	Y-M: 20[redacted] /ONGOING 426
METHYLDOPA	2 TABLETS	TID	Y-M: 20[redacted] /ONGOING 426
NEBIVOLOL	5 mg (milligram(s))	QD	Y-M: 20[redacted] /ONGOING 426

Event #1: Serious Adverse Event

Event Description	ARTHRALGIA
Preferred term	関節痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 131
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 149): ALANINE AMINO TRANSFERASE (SGPT/ALT): 28 [0 - 55] U/L; ALBUMIN: 42 [35 - 52] G/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 23 [5 - 34] U/L; BNP: 21.66 [NOT REPORTED - 100] PG/ML; CHLORIDES: 107 [96 - 106] MMOL/L; CREATININE: 86 [65 - 104] MCMOL/L; ERYTHROCYTE SEDIMENT: 6 [1 - 13] UNIT NOT REPORTED; GLUCOSE: 4.8 [3.9 - 5.5] MMOL/L; HEMATOCRIT: 0.39 [0.42 - 0.5] FRACTION; HEMOGLOBIN: 140 [140 - 175] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 1.1 [0 - 5] MG/L; LDH: 256 [125 - 220] IU/L; MCV: 94 [80 - 96] FL; PLATELET COUNT: 275 [145 - 450] X10^9/L; POTASSIUM: 3.6 [3.5 - 5.2] MMOL/L; RED BLOOD COUNT: 4.2 [4.5 - 5.9] X10^12/L; RHEUMATOID FACTOR: 10.0 [0 - 30] IU/L; SODIUM: 148 [136 - 145] MMOL/L; TOTAL PROTEIN: 64 [65 - 83] G/L; URIC ACID: 266 [208 - 428] MCMOL/L; VITAMIN B12: 117 [187 - 883] PG/ML; WHITE BLOOD COUNT: 6.6 [4.4 - 11.3] X10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 152): FEET X-RAY: NO SIGNIFICANT CHANGE; CHEST X-RAY: NO SIGNIFICANT CHANGE; CHEST X-RAY: NO SIGNIFICANT CHANGE; ABDOMINAL USG: NO SIGNIFICANT CHANGE; ECHOCARDIOGRAPHY: NO SIGNIFICANT CHANGE; [redacted]20[redacted] (RX DAY 154): ECG: NO SIGNIFICANT CHANGE

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HOSPITALISATION DUE TO ARTHRALGIA FOR DIAGNOSTIC AND TREATMENT BETWEEN [redacted]-[redacted]20[redacted]
Discontinued Study Drug Due to the Event	NO

SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	UNCONTROLLED HYPERTENSION
Preferred term	高血圧
AE Onset Date / Rx Day	[redacted]20[redacted] / 420 (63 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 420): BP READING: 205/108 [NOT REPORTED - NOT REPORTED] MMHG; CHLORIDE: 105 [96 - 106] MMOL/L; CREATININE: 74 [65 - 104] MCMOL/L; GLUCOSE: 5.1 [3.9 - 5.5] MMOL/L; HEMOGLOBIN: 159 [140 - 175] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.63 [0 - 5] MG/L; HIGH-SENSITIVITY TRO: 2.0 [NOT REPORTED - 34.2] PG/ML; PLATELET COUNT: 232 [145 - 450] X10^9/L; POTASSIUM: 3.2 [3.5 - 5.2] MMOL/L; RED BLOOD COUNT: 4.6 [4.5 - 5.9] X10^12/L; SODIUM: 143 [136 - 145] MMOL/L; WHITE BLOOD COUNT: 8.2 [4.4 - 11.3] X10^9/L; [redacted]20[redacted] (RX DAY 421): CHOLESTEROL: 4.16 [3.62 - 5.17] MMOL/L; HDL CHOLESTEROL: 32 [40 - NOT REPORTED] MG/DL; LDL CHOLESTEROL: 2.61 [1.81 - 3.36] MMOL/L; TRIGLYCERIDES: 1.55 [0.45 - 1.7] MMOL/L; TSH: 1.74 [0.35 - 4.94] IU/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 420): HEAD CT: NOT CLINICALLY SIGNIFICANT; NEUROLOGISCAL CONSULTATION: WITHIN NORMAL RANGE; [redacted]20[redacted] (RX DAY 421): ECHOCARDIOGRAM: WITHIN NORMAL RANGE; ABDOMEN USG: NOT CLINICALLY SIGNIFICANT; [redacted]20[redacted] (RX DAY 426): CARDIOLOGYST CONSULTATION: HYPERTENSION TREATMENT MODYFICATION

AE Stopped Rx Day	426 (69 DAYS AFTER LAST TREATMENT)
Duration of AE	7 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HOSPITALISATION FOR DIAGNOSIS AND TREATMENT OPTIMALISATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY, LIFE THREATENING

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の関節痛が認められた。関連する病歴は，潰瘍性大腸炎，末梢性顔面神経麻痺，及び右手指の外傷であった。被験者は非喫煙者であり，軽度のアルコール摂取者（1 日当たり 2 ドリンク未満）であった。
20[redacted] 年 [redacted] 月 [redacted] 日，関節痛が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は関節痛の診断検査及び治療のため入院した。入院中，高血圧の治療薬の用量が変更され，ビタミン B12 欠乏が認められたため治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Metypred（メチルプレドニゾロンコハク酸エステルナトリウム）が投与された。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Arthralgia (10003239) (Arthralgia (10003239)) [v.21.1] [10003239]

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 ARTHRALGIA

- Investigator: Hospitalization due to arthralgia for diagnostic and treatment.. Data will be updated when available.

- AbbVie: Risk factors include obesity and pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL USG: NO SIGNIFICANT CHANGE

[redacted] 20[redacted] CHEST X-RAY: NO SIGNIFICANT CHANGE

[redacted] 20[redacted] ECG: NO SIGNIFICANT CHANGE

[redacted] 20[redacted] ECHOCARDIOGRAPHY: NO SIGNIFICANT CHANGE

[redacted] 20[redacted] ERYTHROCYTE SEDIMENT: 6 No units (normal 1 to 13)

[redacted] 20[redacted] FEET X-RAY: NO SIGNIFICANT CHANGE

[redacted] 20[redacted] HEMATOCRIT: 39 % (normal 42 to 50)

[redacted] 20[redacted] HEMOGLOBIN: 14 G/DL (normal 14 to 17.5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 1.10 MG/L (normal 0 to 5)

[redacted] 20[redacted] CHLORIDES: 107 MMOL/L (normal 96 to 106)

[redacted] 20[redacted] LDH: 256 IU/L (normal 125 to 220)

[redacted] 20[redacted] RBC: 4.15 X10**6/MCL (normal 4.5 to 5.9)

[redacted] 20[redacted] RHEUMATOID FACTOR: 10 IU/L (normal 0 to 30)

[redacted] 20[redacted] SODIUM: 148 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] VITAMIN B12: 117 PG/ML (normal 187 to 883)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（ポーランド）であり，重篤な有害事象のコントロールされていない高血圧が認められた。関連する病歴は，左側潰瘍性大腸炎，高血圧，及び非アルコール性脂肪性肝疾患であった。被験者は非喫煙者であり，アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，コントロールされていない高血圧が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，コントロールされていない高血圧は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は高血圧のため入院し，コントロールされていない高血圧と診断された。臨床検査及び画像検査が実施された。循環器内科医及び神経科医による診察が行われた。入院中に被験者の投薬内容が変更され，本事象は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Dopegyt（メチルドパ水和物），Furosemidum（フロセミド），Hydroxizinum，Kalium chloratum，塩化ナトリウム，Nebilet，Tachyben（ウラピジル），及び Triplixam が投与された。

The patient's past medications include:

AMLODIPINUM for HYPERTENSION ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

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

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

PALGOTAL for CHEST PAIN ([redacted] 20[redacted] - [redacted] 20[redacted])

FUROSEMID for LEG EDEMA ([redacted] 20[redacted] - [redacted] 20[redacted])

AXTIL for HYPERTENSION ([redacted] 20[redacted] - [redacted] 20[redacted])

DIURED for HYPERTENSION ([redacted] 20[redacted] - [redacted] 20[redacted])

VITAMIN B12 for DEFICIENCY OF VITAMIN B12 ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Uncontrolled hypertension (10066860) (Hypertension (10020772)) [v.22.0] [10066860]

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 UNCONTROLLED HYPERTENSION

- Investigator: Not Reported

- AbbVie: Event more likely related to pre-existing hypertension.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMEN USG: NOT CLINICALLY SIGNIFICANT

[redacted] 20[redacted] BLOOD PRESSURE: 205/108 mmHg (range: 110/60 - 140/90)

[redacted] 20[redacted] BLOOD PRESURE: 130/90 mmHg

[redacted] 20[redacted] CHOLESTEROL: 161 mg/dL (normal 140 to 200)

[redacted] 20[redacted] CREATININE: 0.84 mg/dL (normal 0.73 to 1.18)

[redacted] 20[redacted] ECHOCARDIOGRAM: WITHIN NORMAL RANGE

[redacted] 20[redacted] GLUCOSE: 91 mg/dL (normal 70 to 99)

[redacted] 20[redacted] HDL: 32 mg/dL (normal <40)

[redacted] 20[redacted] HEAD CT: NOT CLINICALLY SIGNIFICANT

[redacted] 20[redacted] HIGH-SENSITIVITY TRO: 2.0 PG/ML (normal <34.2)

[redacted] 20[redacted] POTASSIUM: 3.17 MMOL/L (normal 3.5 to 5.2)

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
結核	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	2[redacted]	FEMALE	White

Medical History	Onset Year
Not reported.	

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB TDM	40/40 MG	EOW/EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 87	31

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / -167
CALCIUM	1 TABLETS	BID	Y-M: 20[redacted] / -146
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -104
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -69
SULFASALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -69
FERRO-FOLSAN	1 TABLET	QD	Y-M: 20[redacted] / -55
MEBEVERINE	200 mg (milligram(s))	BID	Y-M: 20[redacted] / -55
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / -55
PREDNISONE	40 mg (milligram(s))	Other: DRUG TAKEN IN REGIME: 30MG-10MG-0MG	Y-M: 20[redacted] / -55
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -35
PREDNISONE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / -35
FORTRANS	2 SACHET	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))	TID	Y-M: 20[redacted] / -35	ONGOING
PARACETAMOL	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
AUGMENTIN	1.2 g (gram(s))	TID	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 137
ENOXAPARIN	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 137
FLUCONAZOLE	UNK UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 137
KETOPROFEN	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 137

METOPROLOL	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 137
OMEPRAZOLE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 137
PARACETAMOL	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 137
NATURES WAY PRIMADOPHILUS ORIGINAL	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 1233
CODEINE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
DIAZEPAM	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
ISONIAZID	250 mg (milligram(s))	QD	Y-M: 20[redacted] / 99	ONGOING
PYRAZINAMIDE	1250 mg (milligram(s))	QD	Y-M: 20[redacted] / 99	ONGOING
ETHAMBUTOL	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / 100	ONGOING
RIFAMPICIN	450 mg (milligram(s))	QD	Y-M: 20[redacted] / 100	ONGOING

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

Event Description	TUBERCULOSIS
Preferred term	結核
AE Onset Date / Rx Day	[redacted]20[redacted] / 93 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 93): ALANINE AMINO TRANSFERASE (SGPT/ALT): 12 [5 - 35] U/L; APTT: 30.6 [NOT REPORTED - NOT REPORTED] SEC; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 20 [7 - 40] U/L; C-REACTIVE PROTEIN: 13.44 [NOT REPORTED - NOT REPORTED] MG/L; CREATININE: 47 [53 - 97] MCMOL/L; D-DIMER: 3.83 [NOT REPORTED - NOT REPORTED] UGFEU/ML; FIBRINOGEN: 7.65 [NOT REPORTED - NOT REPORTED] G/L; GLUCOSE: 6.1 [4.1 - 5.9] MMOL/L; HEMATOCRIT: 0.35 [0.35 - 0.45] FRACTION; HEMOGLOBIN: 112 [117 - 155] G/L; INR: 1.07 [NOT REPORTED - NOT REPORTED] RATIO; MCH: 27.4 [NOT REPORTED - NOT REPORTED] PG; MCHC: 31.8 [NOT REPORTED - NOT REPORTED] G/DL; MCV: 86 [NOT REPORTED - NOT REPORTED] FL; MPV: 8.6 [NOT REPORTED - NOT REPORTED] FL; PDW: 13.3 [NOT REPORTED - NOT REPORTED] %; PLATELET COUNT: 432 [150 - 400] X10^9/L; POTASSIUM: 4.4 [3.4 - 4.4] MMOL/L; PROTHROMBIN RATIO: 93 [NOT REPORTED - NOT REPORTED] %; PROTHROMBIN TIME: 10.5 [NOT REPORTED - NOT REPORTED] SEC; RDW-CV: 12.8 [NOT REPORTED - NOT REPORTED] %; RED BLOOD COUNT: 4.1 [3.8 - 5.1] X10^12/L; SODIUM: 136 [136 - 145] MMOL/L; TOTAL BILIRUBIN: 4 [5 - 21] MCMOL/L; UREA: 14.9 [NOT REPORTED - NOT REPORTED] MG/DL; WHITE BLOOD COUNT: 4.9 [4.5 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 94): BE (BASE EXCESS): -0.7 [NOT REPORTED - NOT REPORTED] MMOL/L; CHCO3: 22.8 [NOT REPORTED - NOT REPORTED] MMOL/L; CHCO3ST: 23.8 [NOT REPORTED - NOT REPORTED] MMOL/L; CTCO2: 19.7 [NOT REPORTED - NOT REPORTED] MMOL/L; PCO2: 34.6 [NOT REPORTED - NOT REPORTED] MMHG; PH: 7.437 [NOT REPORTED - NOT REPORTED] RATIO; PO2: 68.0 [NOT REPORTED - NOT REPORTED]

MMHG; SO2: 94 [NOT REPORTED - NOT REPORTED] %; [redacted]20[redacted] (RX DAY 95): GLUCOSE: 78 [NOT REPORTED - NOT REPORTED] MG/L; LDH: 770 [NOT REPORTED - NOT REPORTED] U/L; RIVALTA TEST: POSITIV [NOT REPORTED - NOT REPORTED] NA; SPECIFIC GRAVITY: 1.020 [NOT REPORTED - NOT REPORTED] G/L; TOTAL PROTEIN: 5.2 [NOT REPORTED - NOT REPORTED] G/L; [redacted]20[redacted] (RX DAY 120): ALANINE AMINO TRANSFERASE (SGPT/ALT): 9 [5 - 35] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 16 [7 - 40] U/L; C-REACTIVE PROTEIN: 5.59 [NOT REPORTED - NOT REPORTED] MG/L; CREATININE: 49 [53 - 97] MCMOL/L; D-DIMER: 1.34 [NOT REPORTED - NOT REPORTED] UGFEU/ML; FIBRINOGEN: 6.93 [NOT REPORTED - NOT REPORTED] G/L; GLUCOSE: 4.6 [4.1 - 5.9] MMOL/L; HEMATOCRIT: 0.32 [0.35 - 0.45] FRACTION; HEMOGLOBIN: 103 [117 - 155] G/L; MCH: 26.4 [NOT REPORTED - NOT REPORTED] PG; MCHC: 32.2 [NOT REPORTED - NOT REPORTED] G/DL; MCV: 82 [NOT REPORTED - NOT REPORTED] FL; MPV: 8.8 [NOT REPORTED - NOT REPORTED] FL; PDW: 14.3 [NOT REPORTED - NOT REPORTED] %; PLATELET COUNT: 385 [150 - 400] X10^9/L; POTASSIUM: 4.2 [3.4 - 4.4] MMOL/L; RDW-CV: 13.9 [NOT REPORTED - NOT REPORTED] %; RED BLOOD COUNT: 3.9 [3.8 - 5.1] X10^12/L; SODIUM: 136 [136 - 145] MMOL/L; TOTAL BILIRUBIN: 5 [5 - 21] MCMOL/L; UREA: 15.7 [NOT REPORTED - NOT REPORTED] MG/DL; WHITE BLOOD COUNT: 5.9 [4.5 - 11] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 94): Other SWAB SMEAR FOR MYCOBACTERIUM TUBERCULOSIS: N-NONE; Other PHARYNGEAL SWAB CULTURE: P-STREPTOCOCCUS VIRIDANS-NORMAL FLORA, NEISSERIA SP. - NORMAL FLORA; [redacted]20[redacted] (RX DAY 95): Other PLEURAL FLUID PCR ASSAY FOR THE M. TUBERCULOSIS COMPLE: N-M. TUBERCULOSIS COMPLEX DNA NOT DETECTED; Other PLEURAL FLUID SMEAR FOR MYCOBACTERIUM TUBERCULOSIS: N-NONE; Other SWAB SMEAR FOR MYCOBACTERIUM TUBERCULOSIS: N-NONE; Other FLUID FROM THE PLEURAL CAVITY CULTURE AEROBIC CONDITIONS: N-NONE; [redacted]20[redacted] (RX DAY 98): Other BRONCHIAL WASHING PCR ASSAY FOR THE M. TUBERCULOSIS COMPLE: P-M. TUBERCULOSIS COMPLEX DNA DETECTED; Other BRONCHIAL WASHING SMEAR FOR MYCOBACTERIUM TUBERCULOSIS: N-NONE; Other SWAB SMEAR FOR MYCOBACTERIUM TUBERCULOSIS: N-NONE; Other BRONCHIAL WASHING CULTURE AEROBIC CONDITIONS: N-NONE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 94): CHEST X-RAY PA AND RIGHT LATERAL: RIGHT-SIDED PLEURAL EFFUSION TO THE HEIGHT OF THE ANTERIOR PART OF VI RIB. ABOVE FLUID PULMONARY CONSOLIDATION WITH OPACIFICATION. UPPER RIGHT PULMONARY ZONE, LEFT PULMONARY ZONE AND HEART SILHOUETTE; COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAM: THROMBI IN PULMONARY ARTERIES WERE NOT VISUALIZED. LINEAR STREAK OF ATELECTATIC AND INFLAMMATORY CHANGES ON THE RIGHT MIDDLE PULMONARY LOBE. ENLARGED LYMPHATIC NODES OF RIGHT PULMONARY HILUM (19X15 MM; CHEST ULTRASOUND: MORE THAN 1000 ML OF FLUID IN RIGHT PLEURAL CAVITY. LEFT PLEURAL CAVITY WITHOUT FEATURES OF FLUID AT ULTRASOUND.; [redacted]20[redacted] (RX DAY 98): BRONCHOSCOPY: LARYNX NORMAL. VOCAL CORDS NORMAL, SYMMETRIC, WITHIN THE RIGHT VOCAL CORD SMALL PETECHIAE. IN A BEGINNING PART OF TRACHEA LITTLE PETECHIAE IN MUCOSA. TRACHEA NORMAL. TRACHEAL CARINA SHARP, RESPIRATORY; BRONCHOSCOPY: CD...AT THE RIGHT SIDE ABOVE UPPER LOBE BRONCHUS MUCOSA BLOODSHOT, INFLAMED CHANGED, EASY BLEEDING WHEN TOUCHED BY THE BRONCHOSCOPE. AVAILABLE FOR EXAMINATION BRONCHI UNOBSTRUCTED, UNCHANGED. BRONCHIA; [redacted]20[redacted] (RX DAY 106): CHEST ULTRASOUND: APPROXIMATELY 300 ML OF FLUID IN RIGHT PLEURAL CAVITY. LEFT PLEURAL CAVITY WITHOUT FEATURES OF FLUID AT ULTRASOUND.; [redacted]20[redacted] (RX DAY 121): CHEST X-RAY PA: COMPARED WITH PRIOR STUDY (DATED [redacted]20[redacted]) ALMOST TOTAL REGRESION OF INFLAMMATORY CHANGES IN THE RIGHT INFERIOR PULMONARY ZONE. REMAIN STREAK OPACITIES ON THE PERIPHERAL PART OF THE RIGHT MIDDLE PULM

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING

Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	PATIENTS WITH INCREASED RISK OF DEVELOPING TUBERCULOSIS. THE PATIENT WORKS IN PULMUNOLOGY HOSPITAL.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の結核が認められた。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，結核が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，微熱が認められ，被験者は入院した。発熱（38.5°C）が 1 週間続いており，乾性咳嗽がみられた。咳嗽は過換気の際に悪化した。20[redacted] 年 [redacted] 月 [redacted] 日，胸膜穿刺が実施され，1050 mL の滲出液が排出された。入院中，胸部コンピュータ断層撮影検査及び気管支鏡検査が実施された。結核菌群 DNA の遺伝子検査結果は陽性であり，臨床所見及び画像診断所見，並びに抗 TNF 療法による治療歴に基づき結核と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，イソニアジド，リファンピシン，及びピラジナミドによる抗菌治療が開始された。眼科医による診療後，20[redacted] 年 [redacted] 月 [redacted] 日にエタンブトールが治療薬に追加された。患者の治療に対する忍容性は良好であった。治療中，体温の正常化，咳嗽停止，及び全身状態の改善がみられた。20[redacted] 年 [redacted] 月 [redacted] 日，左下肺領域の炎症性変化がほぼ完全に消退したことが認められた。20[redacted] 年 [redacted] 月 [redacted] 日，患者は良好な全身状態で退院し，退院後も呼吸器内科外来診療所での治療継続が推奨された。

治療薬としてイソニアジド，エタンブトール，リファンピシン，Heligen（オメプラゾール），フルコナゾール，Lacidofil，アセトアミノフェン，Ketonal（ケトプロフェン），Metocard（メトプロロール酒石酸塩），Clexane（エノキサパリンナトリウム），ピラジナミド，及び Amoksiklav 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 (Open Label)

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1) Tuberculosis (10044755) (Tuberculosis (10044755)) [v.19.0] [10044755]

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: No

Alternative Etiology for HUMIRA (Open Label)

Event of TUBERCULOSIS

- Investigator: Patient with increased risk of developing tuberculosis. The patient works in a pulmonology hospital.

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] bronchial wash smear for mycobacterium tuberculosis: negative

[redacted] 20[redacted] bronchial washing culture aerobic conditions: negative

[redacted] 20[redacted] bronchial washing PCR assay for M. Tuberculosis complex DNA: positive m tuberuclosis dna detected

[redacted] 20[redacted] Bronchoscopy:

- larynx normal, vocal cords normal, symmetric, within the right vocal cord small petechiae. In a beginning part of trachea little petechiae in mucosa. Trachea normal. Tracheal carina sharp, respiratory mobile, positioned midline. At the left side mucosa pale, covered little amount of mucosal secretion. Available for examination bronchi unobstructed, unchanged, respiratory mobile. At the right side above upper lobe bronchus mucosa bloodshot, inflamed changed, east bleeding when touched by the bronchoscope. Available for examination bronchi unobstructed, unchanged. Bronchial aspirate was taken for future examinations.

[redacted] 20[redacted] chest ultrasound:

More than 1000 ml of fluid in right pleural cavity. Left pleural cavity without features of fluid on ultrasound.

[redacted] 20[redacted] chest ultrasound:

Approximately 300 ml of fluid in right pleural cavity. Left pleural cavity without features of fluid on ultrasound.

[redacted] 20[redacted] Chest x-ray:

Right sided pleural effusion to the height of the anterior part of VI rib. Above fluid pulmonary consolidation with opacification. Upper right pulmonary zone, left pulmonary zone and heart silhouette within normal limits. left hemidiaphragm with no changes, left costophrenic angle sharp.

[redacted] 20[redacted] chest x-ray PA:

Compared with prior study (dated [redacted] 20[redacted]) almost total regression of inflammatory changes in the righ inferior pulmonary zone. Remain streak opacities on the peripheral part of the right middle pulmonary zone- fibrotic changes? Remained pulmonary zones an heart silhouette within normal limits. Diaphragm with no changes, left costophrenic angle sharp, right costophrenic angle slight obscured-

smaller amount of liquid in the right pleural cavity than previously.

[redacted] 20[redacted] culture aerobic condition: fluid from pleural cavity negative

[redacted] 20[redacted] GLUCOSE: (Fluid from pleural cavity) 78 MG/L

[redacted] 20[redacted] LDH: (Fluid from pleural cavity) 770 U/L

[redacted] 20[redacted] PHARYNGEAL SWAB: Pos streptococcus viridans neisseria sp normal flora

[redacted] 20[redacted] pleural fluid PCR assay for M. Tuberculosis complex DNA: negative

[redacted] 20[redacted] pleural fluid smear for mycobacterium tuberculosis: negative

[redacted] 20[redacted] RIVALTA TEST: (Fluid from pleural cavity) POSITIVE

[redacted] 20[redacted] specific gravity: (Fluid from pleural cavity) 1.020 G/L

[redacted] 20[redacted] swab smear for mycobacterium tuberculosis: negative

[redacted] 20[redacted] swab smear for mycobacterium tuberculosis: negative

[redacted] 20[redacted] swab smear for mycobacterium tuberculosis: negative

[redacted] 20[redacted] TOTAL PROTEIN: (Fluid from pleural cavity) 5.2 G/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	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	2[redacted]	FEMALE	White

Medical History	Onset Year
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: PHARYNGITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB TDM	40/40/40 MG	EOW/EW/EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 232	176

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LOPERAMIDE	4 mg (milligram(s))	PRN	Y-M: 20[redacted]
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -189
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -189
TRIMEBUTINE	100 mg (milligram(s))	TID	Y-M: 20[redacted] / -189
DEXAMETHASONE	3 mg (milligram(s))	QD	Y-M: 20[redacted] / -105
METRONIDAZOLE	0.25 g (gram(s))	QD	Y-M: 20[redacted] / -105
MESALAZINE	1.0 g (gram(s))	TID	Y-M: 20[redacted] / -104
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / -37
ISONIAZID	300 mg (milligram(s))	QD	Y-M: 20[redacted] / -29
FORTRANS	1 SACHET	QD	Y-M: 20[redacted] / -10
MIDAZOLAM	1 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
LOPERAMIDE	4 mg (milligram(s))	PRN	Y-M: 20[redacted]	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -189	ONGOING
MESALAZINE	1.0 g (gram(s))	TID	Y-M: 20[redacted] / -104	Y-M: 20[redacted] / 224
FOLIC ACID	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 44	ONGOING
OTHER NUTRIENTS	1 PORTION	BID	Y-M: 20[redacted] / 174	ONGOING
PANTOPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 204	ONGOING
CARBOHYDRATES NOS W/LIPIDS NOS/PROTEINS NOS	1000 mL (millilitre(s))	QD	Y-M: 20[redacted] / 209	Y-M: 20[redacted] / 225
AMIKACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 212	Y-M: 20[redacted] / 241
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 212	Y-M: 20[redacted] / 241
MESALAZINE	1000 mg (milligram(s))	TID	Y-M: 20[redacted] / 225	ONGOING
ADENOSINE	3 mg (milligram(s))	QD	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 225

ENOXAPARIN	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 250
TRIMEBUTINE	100 mg (milligram(s))	TID	Y-M: 20[redacted] / 229	ONGOING
ADENOSINE	3 mg (milligram(s))	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
METOPROLOL	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 239	ONGOING
AZITHROMYCIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 242	Y-M: 20[redacted] / 272
PANCREATIN	10000 IU (international unit(s))	TID	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 250
PREDNISONE	10 mg (milligram(s))	Other: QD MIDDAY	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 250
VANCOMYCIN	100 mg (milligram(s))	QID	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 250
PREDNISONE	20 mg (milligram(s))	Other: QD MORNING	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 250
ALPRAZOLAM	0.25 mg (milligram(s))	QD	Y-M: 20[redacted] / 247	Y-M: 20[redacted] / 250

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

Event Description	EXACERBATION OF ULCERATIVE COLITIS,
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 225
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 225): HEMATOCRIT: 0.26 [0.36 - 0.48] FRACTION; HEMOGLOBIN: 80 [120 - 160] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 11.6 [0 - 6] MG/L; PLATELET COUNT: 795 [150 - 400] X10^9/L; RED BLOOD COUNT: 3 [3.8 - 5.4] X10^12/L; WHITE BLOOD COUNT: 13.4 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 226): HEMATOCRIT: 0.23 [0.36 - 0.48] FRACTION; HEMOGLOBIN: 73 [120 - 160] G/L; PLATELET COUNT: 841 [150 - 400] X10^9/L; RED BLOOD COUNT: 2.6 [3.8 - 5.4] X10^12/L; WHITE BLOOD COUNT: 9.4 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 228): PLATELET COUNT: 647 [150 - 400] X10^9/L; [redacted]20[redacted] (RX DAY 232): PLATELET COUNT: 662 [150 - 400] X10^9/L; [redacted]20[redacted] (RX DAY 236): PLATELET COUNT: 645 [150 - 400] X10^9/L; [redacted]20[redacted] (RX DAY 237): PLATELET COUNT: 585 [150 - 400] X10^9/L; [redacted]20[redacted] (RX DAY 238): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 29.9 [0 - 6] MG/L; PLATELET COUNT: 519 [150 - 400] X10^9/L; [redacted]20[redacted] (RX DAY 240): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 13 [0 - 6] MG/L; PLATELET COUNT: 483 [150 - 400] X10^9/L; [redacted]20[redacted] (RX DAY 243): PLATELET COUNT: 502 [150 - 400] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 232): Stool C. DIFF QUICK CHECK AND TOX A/B QUICK CH: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 225): ECG: NORMAL; [redacted]20[redacted] (RX DAY 226): PACKED RED BLOOD CELL TRANSFUSION: ANEMIA IMPROVED, NO ADVERSE REACTION; [redacted]20[redacted] (RX DAY 231): CT ABDOMEN

BIPHASIC: THICKENED WALL OF THE RECTUM, THE SIGMOID AND THE DESCENDING COLON UP TO 8 MM, WITH CONTRAST ENHANCEMENT OF THE MUCOSA - FEATURES OF INFLAMMATION; NARROW INTESTINAL LUMEN.; COLONOSCOPY: INFLAMMATORY CHANGES IN THE DISTAL PORTION OF THE COLON, THE MUCOSA WAS SWOLLEN WITH EROSIONS AND A FLAT ULCERATION.

AE Stopped Rx Day	250 (18 DAYS AFTER LAST TREATMENT)
Duration of AE	26 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	LACK OF STUDY DRUG EFFICIENCY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[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，左側潰瘍性大腸炎であった。

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，被験者は重篤な潰瘍性大腸炎の増悪（Mayo スコア 9）のため入院した。二次性（深在性）貧血，血小板増加症，白血球増加症，肝血管腫，及び発作性心室性頻脈（200 bpm）を含む症状が認められた。また，アルブミン低値，総たん白量低値，及び C 反応性たん白値のわずかな上昇（11.6 mg/L）を含む所見が認められた。コンピュータ断層撮影検査が実施された結果，結腸の遠位部に炎症性変化がみられ，粘膜が腫脹してびらんが生じており，扁平性の潰瘍形成が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師は，被験者の頻脈は貧血によるものと述べた。

治療薬として Debretin，Betaloc ZOK 50，パンクレアチン，Encorton，Alpragen，赤血球濃厚液，メトロニダゾール，アジスロマイシン，Adenocor，Acidum Folicum，Asamax（メサラジン）500，Clexane（エノキサパリンナトリウム），アルブミン，Edicin，及び Biodacyna（アミカシン）が投与された。

The patient's past medications include:

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

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

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

- Investigator: Lack of study drug efficiency

- AbbVie: THE EVENT IS EXACERBATION OF UNDERLYING DISEASE.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] C DIFFICILE: NEGATIVE

thickened wall of the rectum, the sigmoid and the descending colon up to

8 mm, with contrast enhancement of the mucosa - features of inflammation; narrow intestinal lumen.

[redacted] 20[redacted] COLONOSCOPY:

[redacted] 20[redacted] CT:

- inflammatory changes in the distal portion of the colon, the mucosa was swollen with erosions and a flat ulceration was identified.

[redacted] 20[redacted] EKG: NORMAL

[redacted] 20[redacted] HEMATOCRIT: 26.0 % (normal 36.0 to 48.0)

[redacted] 20[redacted] HEMOGLOBIN: 8.0 G/DL (normal 12.0 to 16)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 29.9 (normal 0.0 to 6.0)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 13.0

[redacted] 20[redacted] NEUTROPHILS: 9.20 X10**3/MM**3 (normal 2.20 to 4.80)

[redacted] 20[redacted] PLATELET COUNT: 795 X10**3/MCL (normal 150 to 400)

[redacted] 20[redacted] PLATELET COUNT: 502 X10**3/MM**3

[redacted] 20[redacted] WBC: 13.41 X10**3/MCL (normal 4 to 11)

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
肺炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
ANEMIA: ANEMIA WITH IRON DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 55	[redacted]20[redacted] / 357	303

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AIDA	1 TABLET	Other: QD PER 21DAYS AND 7 DAYS BREAKE	Y-M: 20[redacted]
IRON	1 TABLET	QD	Y-M: 20[redacted] / -99
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -98
CALCIUM DOBESILATE	250 mg (milligram(s))	BID	Y-M: 20[redacted] / -98
FOLIC ACID	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -98
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -98
MESALAZINE	1.5 g (gram(s))	BID	Y-M: 20[redacted] / -98
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -98
TRIMEBUTINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -98
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] / -46
COLECALCIFEROL	6 gtt (drop(s))	QD	Y-M: 20[redacted] / -29
PICO-SALAX	1 SACHET	QD	Y-M: 20[redacted] / -16
FENTANYL	0.05 mg (milligram(s))	QD	Y-M: 20[redacted] / -15

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
AIDA	1 TABLET	Other: QD PER 21DAYS AND 7 DAYS BREAKE	Y-M: 20[redacted]	ONGOING
IRON	1 TABLET	QD	Y-M: 20[redacted] / -99	ONGOING
CALCIUM DOBESILATE	250 mg (milligram(s))	BID	Y-M: 20[redacted] / -98	ONGOING
FOLIC ACID	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -98	ONGOING

MESALAZINE	1.5 g (gram(s))	BID	Y-M: 20[redacted] ONGOING / -98
TRIMEBUTINE	1 g (gram(s))	TID	Y-M: 20[redacted] ONGOING / -98
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] ONGOING / -46
COLECALCIFEROL	6 gtt (drop(s))	QD	Y-M: 20[redacted] ONGOING / -29
FENTANYL	0.1 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 55 55
CEFTRIAXONE	1 g (gram(s))	BID	Y-M: 20[redacted] Y-M: 20[redacted] / / 68 75

Event #1: Serious Adverse Event

Event Description	RIGHT SIDE PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 65
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 68): HEMOGLOBIN: 118 [117 - 155] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 92.45 [NOT REPORTED - NOT REPORTED] MG/L; WHITE BLOOD COUNT: 17.8 [4.5 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 75): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 1.03 [NOT REPORTED - NOT REPORTED] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 68): X-RAY: PULMONARY FIELDS WITHOUT FOCAL LESIONS. DIAPHRAGM IN NORMAL. CARDIAC SILHOUETTE WITHIN NORMAL LIMITS.; ELECTROCARDIOGRAM: SINUS RHYTHM-100/MIN (NORMAL)

AE Stopped Rx Day	75
Duration of AE	11 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の右側肺炎が認められた。関連する病歴は，左側潰瘍性大腸炎及び鉄欠乏貧血であった。

20[redacted] 年 [redacted] 月 [redacted] 日，右側肺炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，右側肺炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，発熱（39°C），持続性咳嗽，及び 2～3 日間続く脱力の兆候及び症状が認められ，被験者は入院した。臨床検査の結果，C 反応性たん白値は 92.45 mg/L，白血球数は 17.78×10^3 /μL であった。入院中に診断検査が行われ，抗生剤を含む薬物療法が実施された。臨床状態は著しく改善した。入院期間中に合併症は認められなかった。患者の全身状態は良好であった。20[redacted] 年 [redacted] 月 [redacted] 日，以下に示す推奨事項が提示され，被験者は退院した。1．外来治療：プライマリケア外来診療所における全身管理，2．消化器科外来診療所における治療の継続，3．感染症への曝露の回避。

治験責任医師により，本事象に関連した被験者のリスク因子は治験薬による生物学的治療及び GKS であると判断された。

治療薬として Biotrakson が投与された。

The patient's past medications include:

CORTIMENT MMX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Pneumonia(10035664) (Pneumonia (10035664)) [v.19.1] [10035664]

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 40MG/0.8ML (Open Label)

Event of RIGHT SIDE PNEUMONIA

- Investigator: N/A

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] 20[redacted] CRP: 92.45 MG/L

[redacted] 20[redacted] CRP: 1.03 MG/L

[redacted] 20[redacted] ECG: Sinus rhythm- 100/min (normal)

[redacted] 20[redacted] HEMOGLOBIN: 11.8 G/DL

[redacted] 20[redacted] XRAY: Pulmonary fields without focal lesions. Diaphragm in normal. Cardiac silhouette within normal limits.

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
膀胱癌	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	7[redacted]	MALE	White

Medical History	Onset Year
HYPERTENSION: HYPERTENSION	20[redacted]
OTHER: DISLIPIDEMIA	20[redacted]
SURGERY: PROSTATECTOMY	20[redacted]
OTHER: ESOPHAGAL INFLAMMATION	20[redacted]
OTHER: GASTRITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	40	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB 4040 MG		EW	[redacted]20[redacted] /	[redacted]20[redacted] /	92

MG EVERY WEEK	56	147

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LOPERAMIDE	2 g (gram(s))	PRN	Y-M: 20[redacted]
SIMVASTATIN	10 mg (milligram(s))	QD	Y-M: 20[redacted]
LISINOPRIL	5 mg (milligram(s))	QD	Y-M: 20[redacted]
BUTYRIC ACID	1 CAPSULE	BID	Y-M: 20[redacted] / -356
CALCIUM DOBESILATE	1 TABLET	BID	Y-M: 20[redacted] / -356
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -235
SULFASALAZINE	1000 mg (milligram(s))	TID	Y-M: 20[redacted] / -235
POTASSIUM	600 mg (milligram(s))	QD	Y-M: 20[redacted] / -204
TORASEMIDE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -204
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -174
PREDNISONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -37
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -37
FORTRANS	2 SACHETS	QD	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
LOPERAMIDE	2 g (gram(s))	PRN	Y-M: 20[redacted]	ONGOING
SIMVASTATIN	10 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
LISINOPRIL	5 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
BUTYRIC ACID	1 CAPSULE	BID	Y-M: 20[redacted] / -356	ONGOING
CALCIUM DOBESILATE	1 TABLET	BID	Y-M: 20[redacted] / -356	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -235	ONGOING
SULFASALAZINE	1000 mg (milligram(s))	TID	Y-M: 20[redacted] / -235	ONGOING
POTASSIUM	600 mg (milligram(s))	QD	Y-M: 20[redacted] / -204	ONGOING
TORASEMIDE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -204	ONGOING

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

Event Description	BLADDER CANCER
Preferred term	膀胱癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 120
Age at AE Onset	7[redacted]

Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
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	NEW MEDICAL EVENT
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，7[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の膀胱癌が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）及び前立腺摘除術であった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 40 年）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，膀胱癌が認められた。

本事象により治験薬投与は中止された。被験者は繊維工場勤務及び元喫煙者のリスク因子を有していた。

尿に血液が混じる赤血球尿が認められたため，被験者は泌尿器科医による診察を受けた。被験者は膀胱鏡検査の適応となり，検査の結果，膀胱に変化が認められた。腹腔鏡下切除術の治療が行われた。

The patient's past medications include:

FORTRANS for ENDOSCOPY PREPARATION and ENDOSCOPY PREPARATION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Bladder cancer (10005003) (Bladder cancer (10005003)) [v.20.0] [10005003]

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 BLADDER CANCER

- Investigator: New medical event.

- AbbVie: Present risk factors: age and long smoking history.

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			
クロストリジウム・ディフィシレ感染	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK2[redacted]		FEMALE	White

Medical History	Onset Year
OTHER: MENSTRUAL DISORDERS	20[redacted]
OTHER: HYPOTHYROIDISM	20[redacted]
OTHER: RIGHT KIDNEY CYST	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44
ADALIMUMAB 4040 MG MG EVERY		EOW	[redacted]20[redacted] / 60	[redacted]20[redacted] / 158	99

OTHER WEEK

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LEVOTHYROXINE	25 mcg (microgram(s))	Other: EVERY OTHER WEEK	Y-M: 20[redacted] / -313
DROTAVERINE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / -130
ESOMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -130
PREDNISONE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / -130
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -113
MESALAZINE	4,5 g (gram(s))	QD	Y-M: 20[redacted] / -113
SUPREP BOWEL PREP	176 mL (millilitre(s))	BID	Y-M: 20[redacted] / -16

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
LEVOTHYROXINE	25 mcg (microgram(s))	Other: EVERY OTHER WEEK	Y-M: 20[redacted] / -313	ONGOING
DROTAVERINE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / -130	ONGOING
ESOMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -130	ONGOING
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -113	ONGOING
MESALAZINE	4,5 g (gram(s))	QD	Y-M: 20[redacted] / -113	ONGOING
IRON	325 mg (milligram(s))	QD	Y-M: 20[redacted] / 48	ONGOING
DROTAVERINE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 119
GLUCOSE	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 119
LEVOTHYROXINE	50 mcg (microgram(s))	QD	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 119
SODIUM CHLORIDE	500 mL (millilitre(s))	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 119
RED BLOOD CELLS	UNK mL (millilitre(s))	TID	Y-M: 20[redacted] / 160	Y-M: 20[redacted] / 160
SODIUM CHLORIDE	500 mL (millilitre(s))	BID	Y-M: 20[redacted] / 160	Y-M: 20[redacted] / 164

LEVOTHYROXINE	50 mcg (microgram(s))	QD	Y-M: 20[redacted] / 160	Y-M: 20[redacted] / 174
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 160	Y-M: 20[redacted] / 174
IRON	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 162
PAPAVERINE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 162
VANCOMYCIN	250 mg (milligram(s))	QID	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 174

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF UC.
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 117
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 117): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 12 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 118): Stool CLOSTRIDIUM DIFFCIALE TEST: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 117): HISTOPATHOLOGY: NO EVIDENCE OF CRYPTITIS; RECTOSCOPY: MUCOSA SWOLLEN, FRAGILE, SPONTANEOUSLY, HEMORRHAGIC (MAYO 2)

AE Stopped Rx Day	119
Duration of AE	3 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	CLOSTRIDIUM DIFFICILE INFECTION
Preferred term	クロストリジウム・ディフィシレ感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 160 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 160): HEMOGLOBIN: 70 [110 - 150] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 49.2 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 161): C.DIFFICILE TOXIN A: POSITIVE [NOT REPORTED - NOT REPORTED]

POSITIVE OR NEGATIVE

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 160): BLOOD TRANSFUSION (RED BLOOD CELLS CONCE: TREATMENT OF ANEMIA (SUCCESSFUL); TPN: TREATMENT (SUCCESSFUL); [redacted]20[redacted] (RX DAY 162): RECTOSCOPY: SYMPTOMS TYPICAL OF MAYO 3; [redacted]20[redacted] (RX DAY 168): RTG ABDOMINAL: NORMAL; RTG CHEST AP: NORMAL

AE Stopped Rx Day	174 (16 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	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[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，潰瘍性大腸炎であった。

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。下痢，腹痛，潰瘍性大腸炎の増悪による脱力が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。臨床検査が実施され，結果は正常であった。静脈内輸液が行われた。直腸鏡検査の結果，特発性出血を伴う易出血性の粘膜腫脹が認められた。また，組織学的検査の結果，陰窩炎の所見は認められなかった。

治療薬として塩化ナトリウム注射液，ブドウ糖 5%，及び Natrium Citricum 0.9%が投与された。

The patient's past medications include:

CONTROLOC (PANTOPRAZOL) for STOMACH ACHE ([redacted] 20[redacted] - [redacted] 20[redacted])

CYCLONAMINE 12.5% for BLOODY DIARRHEA ([redacted] 20[redacted] - [redacted] 20[redacted])

PAPAVERINUM for STOMACH ACHE ([redacted] 20[redacted] - [redacted] 20[redacted])

TRAMADOL for STOMACH ACHE ([redacted] 20[redacted] - [redacted] 20[redacted])

CORHYDRONE for C. DIFF INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted])

COSMOFER (FERRUM) for ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

KABIVEN (TPN) for WEAKNESS, NAUSEA and LOSS OF APPETITE ([redacted] 20[redacted] - [redacted] 20[redacted])

METRONIDAZOL for CLOSTRIDIUM DIFFICILE INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted])

PARACETAMOL for C. DIFF INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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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: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of EXACERBATION OF UC

- Investigator: ULCERATIVE COLITIS

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] C-reactive protein: 12 MG/L (normal 0 to 5)

[redacted] 20[redacted] Stool - clostridium diffcile test: Negative
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（ポーランド）であり，重篤な有害事象のクロストリジウム・ディフィシレ感染が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。
20[redacted] 年[redacted] 月[redacted] 日，クロストリジウム・ディフィシレ感染が認められた。20[redacted] 年[redacted] 月[redacted] 日，クロストリジウム・ディフィシレ感染は回復した。20[redacted] 年[redacted] 月[redacted] 日，被験者は入院した。被験者は腹痛，発熱，及び血液が混じった下痢を訴えた。身体的診察では，腹部の圧痛及び皮膚の蒼白が認められた。20[redacted] 年[redacted] 月[redacted] 日，高カロリー輸液が実施された。20[redacted] 年[redacted] 月[redacted] 日，直腸鏡検査が実施され，「Mayo スコア 3」の典型的症状が認められた。入院中，被験者はクロストリジウム・ディフィシレ感染と診断された。20[redacted] 年[redacted] 月[redacted] 日，腹部及び胸部の X 線検査所見は正常であった。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。
治療薬として CosmoFer，濃厚赤血球，バンコマイシン，Encorton，0.9 %塩化ナトリウム溶液，及び Papaverinum（パパベリン）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])

CONTROLOC (PANTOPRAZOL) for STOMACH ACHE ([redacted] 20[redacted] - [redacted] 20[redacted])

CYCLONAMINE 12.5% for BLOODY DIARRHEA ([redacted] 20[redacted] - [redacted] 20[redacted])

PAPAVERINUM for STOMACH ACHE ([redacted] 20[redacted] - [redacted] 20[redacted])

TRAMADOL for STOMACH ACHE ([redacted] 20[redacted] - [redacted] 20[redacted])

CORHYDRONE for EXACERBATION OF ULCERATIVE COLITIS BECAUSE OF CLOSTRIDIUM DI ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Clostridium difficile infection (10054236) (Clostridium difficile infection (10054236)) [v.20.0] [10054236]

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 CLOSTRIDIUM DIFFICILE INFECTION

- Investigator: Not reported.

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HEMOGLOBIN: 7.0 G/DL (normal 11.0 to 15.0)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 49.2 MG/L (normal 0 to 5)

[redacted] 20[redacted] RECTOSCOPY: SYMPTOMS TYPICAL OF MAYO 3

[redacted] 20[redacted] STOOL CULTURE: C.DIFFICILE TOXIN A-POSITIVE

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 TDM	2[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: ATOPIC DERMATITIS	19[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB TDM	40/40/40 MG	EOW/EOW/EW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 197	140

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LEVONORGESTREL	1 IUD	Other: ALL THE TIME	Y-M: 20[redacted]
CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / -297
MERCAPTOPURINE	75 mg (milligram(s))	QD	Y-M: 20[redacted] / -297
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -297
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -144
SUPREP BOWEL PREP	176 mL (millilitre(s))	BID	Y-M: 20[redacted] / -18

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LEVONORGESTREL	1 IUD	Other: ALL THE TIME	Y-M: 20[redacted]	ONGOING
CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / -297	ONGOING
MERCAPTOPURINE	75 mg (milligram(s))	QD	Y-M: 20[redacted] / -297	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -144	ONGOING
DALTEPARIN	5000 IU (international unit(s))	QD	Y-M: 20[redacted] / 200	Y-M: 20[redacted] / 211
DEXAMETHASONE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / 200	Y-M: 20[redacted] / 211
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 200	Y-M: 20[redacted] / 211
MORPHINE	5 mg (milligram(s))	BID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 205
METAMIZOLE	2,5 g (gram(s))	BID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 208
SODIUM CHLORIDE	500 mL (millilitre(s))	BID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 208
AUGMENTIN	1,2 g (gram(s))	BID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 211
TRAMADOL	100 mg (milligram(s))	BID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 211

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

Event Description	EXACERBATION COLITIS ULCEROSA
Preferred term	潰瘍性大腸炎

AE Onset Date / Rx Day	[redacted]20[redacted] / 200 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 200): HEMATOCRIT: 0.33 [0.37 - 0.47] FRACTION; HEMOGLOBIN: 106 [110 - 150] G/L; [redacted]20[redacted] (RX DAY 208): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 140.2 [0 - 5] MG/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 201): COLONOSCOPY: MAYO 3; [redacted]20[redacted] (RX DAY 204): SURGICAL TREATMENT OF ULCERATIVE COLITIS: ILEORECTO J-POUCH ANASTOMOSIS	
AE Stopped Rx Day	211 (14 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	EXACERBATION COLITIS ULCEROSA
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[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，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）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，被験者は潰瘍性大腸炎の外科治療実施ため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，大腸内視鏡検査の結果，Mayo スコア 3 であることが分かった。潰瘍性大腸炎の増悪（血液が混じった下痢，腹痛，及び発熱）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，J 型回腸嚢直腸吻合術が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として塩化ナトリウム，Pyralgin，Poltram（トラマドール塩酸塩），及びモルヒネが投与された。

The patient's past medications include:

ENCORTON for COLITIS ULCEROSA ([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 (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: No

Alternative Etiology for HUMIRA (Open Label)

Event of EXACERBATION COLITIS ULCEROSA

- Investigator: Exacerbation colitis ulcerosa.

- AbbVie: The event is exacerbation of underlying disease of UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] colonoscopy: Mayo 3

[redacted] 20[redacted] HEMATOCRIT: 32.9 % (normal 37 to 47)

[redacted] 20[redacted] HEMOGLOBIN: 10.6 G/DL (normal 11 to 15)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 140.2 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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	2[redacted]	FEMALE	White

Medical History	Onset Year
Not reported.	

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 148	92

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.5 g (gram(s))	QD	Y-M: 20[redacted]
MARVELON	1 TABLET	QD	Y-M: 20[redacted] / -223
CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / -72
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -72
SUPREP BOWEL PREP	176 mL (millilitre(s))	BID	Y-M: 20[redacted] / -18
SUPREP BOWEL PREP	176 mL (millilitre(s))	BID	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
MESALAZINE	4.5 g (gram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 148
MARVELON	1 TABLET	QD	Y-M: 20[redacted] / -223	ONGOING
CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / -72	ONGOING
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 155
HYDROCORTISONE	200 mg (milligram(s))	BID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 155
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 155

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

Event Description	EXACERBATION COLITIS ULCEROSA
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 149 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 149): FERRUM: 16 [60 - 180] MCG/DL; HEMOGLOBIN: 87 [110 - 150] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 235.2 [0 - 5] MG/L; WHITE BLOOD COUNT: 14.8 [4 - 10] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 151): Stool TEST FOR CLOSTRIDIUM DIFFICILE INFECTION: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 149): X-RAY ABDOMINAL: NO CHANGE; [redacted]20[redacted] (RX DAY 151): RECTOSCOPY: MAYO 3

AE Stopped Rx Day	155 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	7 DAYS

Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	EXACERBATION COLITIS ULCEROSA
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[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，潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。
被験者は脱力，動悸，血液が混じった下痢，腹痛，及び熱っぽさのため病院を受診した。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に入院し，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。
治療薬として Hydrocortisonum（Corthydron），シプロフロキサシン，及びメトロニダゾールが投与された。

Causality for HUMIRA (Open Label)

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1) Colitisulcerative 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: No

Alternative Etiology for HUMIRA (Open Label)

Event of EXACERBATION COLITIS ULCEROSA

- Investigator: Exacerbation colitis ulcerosa

- AbbVie: The event is exacerbation of underlying disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Clostridium Difficile: Negative

[redacted] 20[redacted] Colonoscopy:

Colonoscopy Screening

Rectum: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Sigmoid: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Descending colon: 1= Mild disease(erythema, decreased vascular pattern, mild friability)

Transverse colon: 1= Mild disease(erythema, decreased vascular pattern, mild friability)

Ascending colon/cecum: 0 = Normal or inactive disease

Friability is present; Subscore: 2

[redacted] 20[redacted] ferrum: 16 MCG/DL (normal 60 to 180)

[redacted] 20[redacted] FLexible sigmoidoscopy:

Week 8 Flexible sigmoidoscopy

Rectum: 1= Mild disease (erythema, decreased vascular pattern, mild friability)

Sigmoid: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Descending colon: 1= Mild disease(erythema, decreased vascular pattern, mild friability)

Friability is not present; Subscore: 2

[redacted] 20[redacted] Hemoglobin: 8.7 G/DL (normal 11 to 15)

[redacted] 20[redacted] High Sensitivity C-reactive protein: 235.2 MG/L (normal 0 to 5)

[redacted] 20[redacted] Rectoscopy: Mayo 3

[redacted] 20[redacted] WBC: 14.77 X10**3/MCL

[redacted] 20[redacted] X-Ray abdominal: No Change

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
結核	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: TONSILLECTOMY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 161	106

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	293 mg (milligram(s))	Other: ACCORDING TO THE RECOMMENDATION	Y-M: 20[redacted]
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted]
EVRA	1 ADHESIVE PLASTER	Other: ONCE FOR A WEEK	Y-M: 20[redacted] / -128
SUPREP BOWEL PREP	176 mL (millilitre(s))	BID	Y-M: 20[redacted] / -9

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 173
EVRA	1 ADHESIVE PLASTER	Other: ONCE FOR A WEEK	Y-M: 20[redacted] / -128	ONGOING
ACETYLCYSTEINE	600 mg (milligram(s))	QD	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
CIPROFLOXACIN	200 mg (milligram(s))	BID	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
DALTEPARIN	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
METAMIZOLE	UNKNOWN UNKNOWN	PRN	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
METOCLOPRAMIDE	UNKNOWN UNKNOWN	PRN	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
METOPROLOL	50 mg (milligram(s))	BID	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
PARACETAMOL	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
PROMETHAZINE	10+25 mg (milligram(s))	Other: 10+25MG	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
THIOCODIN	(15+300)X1 mg (milligram(s))	QD	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 189
AUGMENTIN	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 190

CEFTRIAXONE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 174 190
FLUCONAZOLE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 174 190
LACTOBACILLUS ACIDOPHILUS	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 174 190
LOPERAMIDE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 174 190
METRONIDAZOLE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 174 190
SACCHAROMYCES BOULARDII	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 174 190
SACCHAROMYCES BOULARDII	250 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 174 193
RIFINAH	(300+150)X2 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 185 268
ETHAMBUTOL	1250 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 189 192
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / ONGOING 190
PREDNISONE	0.02 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / ONGOING 190
AMIKACIN	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 190 193
BUDESONIDE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 190 193
NATURES WAY PRIMADOPHILUS ORIGINAL	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 190 193
THIOCODIN	(15+300)X2 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 190 193
PANTOPRAZOLE	0.02 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 190 214
PYRAZINAMIDE	0.5 g (gram(s))	TID	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 190 268
ETHAMBUTOL	0.25 g (gram(s))	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 191 193
CODEINE	UNK UNK	PRN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 193 214
LACTOBACILLUS ACIDOPHILUS	UNK UNK	PRN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 193 214
METAMIZOLE	UNK UNK	PRN	Y-M: 20[redacted]-[redacted] / Y-M: 20[redacted]-[redacted] / 193 214

OMEPRAZOLE	UNK UNK	PRN	Y-M: 20[redacted] / Y-M: 20[redacted] / 193 214
PARACETAMOL	UNK UNK	PRN	Y-M: 20[redacted] / Y-M: 20[redacted] / 193 214
ETHAMBUTOL	750 mg (milligram(s))	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 193 268

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

Event Description	TUBERCULOSIS
Preferred term	結核
AE Onset Date / Rx Day	[redacted]20[redacted] / 174 (13 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 190): ALANINE AMINO TRANSFERASE (SGPT/ALT): 38 [0 - 35] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 74 [0 - 35] U/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 99.81 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 175): URINE: URINARY TRACT INFECTION; [redacted]20[redacted] (RX DAY 190): RTG CHECT: CHANGES TYPICAL TUBERCULOSIS; [redacted]20[redacted] (RX DAY 191): BRONCHIAL CLIPPINGS: NO PROBLEMS WITH BRONCHIAL CLIPPINGS

AE Stopped Rx Day	268 (107 DAYS AFTER LAST TREATMENT)
Duration of AE	95 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の結核が認められた。関連する病歴は潰瘍性大腸炎であり，被験者は非喫煙者であった。
20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な咽喉痛，乾性咳嗽，発熱が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，結核が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者から咳嗽，呼吸困難，及び身体能力の低下の報告があった。入院中，被験者は結核と診断された。臨床検査が実施され，薬物治療が行われた。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
20[redacted] 年 [redacted] 月 [redacted] 日，結核は回復した。
治療薬として Enterol，Asamax（メサラジン），Cortiment，Fragmin（ダルテパリンナトリウム），Pyralgin，Thiocodin，Metocard（メトプロロール酒石酸塩），アセトアミノフェン，Cipronex（シプロフロキサシン），Metoclopramidum（メトクロプラミド），ロペラミド，Diphergan，ACC，Biotrakson，メトロニダゾール，Mycomax，Rifamazid Forte，エタンブトール，Pentasa（メサラジン），アミカシン，Controloc 20，Encorton，Lacidofil，ピラジナミド，Lakcid，及び Augmentin（クラブラン酸カリウム／アモキシシリン水和物）が投与された。

Causality for HUMIRA (Blinded)

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1) Tuberculosis (10044755) (Tuberculosis (10044755)) [v.20.0] [10044755]

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 TUBERCULOSIS

- Investigator: N/A

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Bronchial clippings: positive

[redacted] 20[redacted] C-reactive protein: 99.81 MG/L

[redacted] 20[redacted] RTG CHEST: changes typical tuberculosis

[redacted] 20[redacted] SGOT/AST: 73.8 U/L (normal 0 to 35)

[redacted] 20[redacted] SGPT/ALT: 38 U/L (normal 0 to 35)

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
クロストリジウム・ディフィシレ感染	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	MALE	White

Medical History	Onset Year
PRIMARY SCLEROSING CHOLANGITIS: PRIMARY SCLEROSING CHOLANGITIS	20[redacted]
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 46	46
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 361	305

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1 g (gram(s))	Other: FOUR TIMES PER DAY	Y-M: 20[redacted]
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]
MERCAPTOPURINE	75 mg (milligram(s))	QD	Y-M: 20[redacted]
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]
URSODEOXYCHOLIC ACID	750 mg (milligram(s))	QD	Y-M: 20[redacted] / -200
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -84
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / -84
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -84
SUPREP BOWEL PREP	176 mL (millilitre(s))	BID	Y-M: 20[redacted] / -15

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
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
URSODEOXYCHOLIC ACID	750 mg (milligram(s))	QD	Y-M: 20[redacted] / -200	Y-M: 20[redacted] / 216
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -84	ONGOING
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -84	Y-M: 20[redacted] / 216
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 218
HYDROCORTISONE	200 mg (milligram(s))	BID	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 218
PERIKABIVEN	1920 mL (millilitre(s))	QD	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 218
SODIUM CHLORIDE	500 mL (millilitre(s))	BID	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 221
IRON	1 gtt (drop(s))	QD	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 225
URSODEOXYCHOLIC ACID	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 225
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 218	Y-M: 20[redacted] / 231
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 219	Y-M: 20[redacted] / 225

PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted]- / 226	ONGOING
URSODEOXYCHOLIC ACID	750 mg (milligram(s))	QD	Y-M: 20[redacted]- / 226	ONGOING

Event #1: Serious Adverse Event

Event Description	CLOSTRIDIUM DIFFICILE INFECTION
Preferred term	クロストリジウム・ディフィシレ感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 217
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 217): ALP: 116 [30 - 120] U/L; ALT: 40 [NOT REPORTED - 45] U/L; APTT: 30.3 [24 - 35] SEC; AST: 21 [NOT REPORTED - 35] U/L; CREATININE: 115 [71 - 106] MCMOL/L; GLUCOSE: 9 [4.1 - 5.9] MMOL/L; POTASSIUM: 4.3 [3.5 - 5.1] MMOL/L; SODIUM: 132 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 218): FERRUM: 7 [70 - 180] MCG/DL; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 47.3 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 222): HEMOGLOBIN: 89 [120 - 170] G/L

Microbiology

[redacted]20[redacted] (RX DAY 218): Stool TOXIN A AND B OF CLOSTRIDIUM DIFFICILE: P

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 217): ECG: THE NORMAL RANGE; X-RAY OF ABDOMEN: ENLARGED INTESTINAL LOOPS WERE NOT SEEN. SINGLE LEVELS OF FLUIDS WERE EXPOSED INSIDE INTESTINAL LOOPS.; X-RAY CHEST: IN THE PERIPHERAL PART OF THE CENTER AREA OF LEFT LUNG, THERE IS A SLIGHTLY VISIBLE SHADOW (DIAMETER: 13 MM) BELOW FRONT SECTION IV RIB.; [redacted]20[redacted] (RX DAY 218): RECTOSCOPY: COLITIS (MAYO 3)

AE Stopped Rx Day	231
Duration of AE	15 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HOSPITALIZATION DUE TO C.DIFFICILE INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象のクロストリジウム・ディフィシレ感染が認められた。関連する病歴は，潰瘍性大腸炎（全大腸炎型）であった。
20[redacted] 年 [redacted] 月 [redacted] 日，クロストリジウム・ディフィシレ感染が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。下痢，腹痛，及び脱力の兆候及び症状が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，クロストリジウム・ディフィシレ感染は回復した。
治験薬投与開始前の 20[redacted] 年 [redacted] 月に，クロストリジウム・ディフィシレ感染が認められていた。
治療薬として Kabiven，Cipronex（シプロフロキサシン），メトロニダゾール，0.9 %塩化ナトリウム溶液，Ascofer，Proursan，Corhydron，及び Encorton が投与された。

The patient's past medications include:

ECORTON for COLITIS ULCEROSA ([redacted] 20[redacted] - [redacted] 20[redacted])

ENCORTON for COLITIS ULCEROSA (Started [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], Stopped [redacted] 20[redacted])

METRONIDAZOL for CLOSTRIDIUM DIFFICILE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Clostridium difficile infection (10054236) (Clostridium difficile infection (10054236)) [v.19.1] [10054236]

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 (Open Label)

Event of CLOSTRIDIUM DIFFICILE INFECTION

- Investigator: Hospitalization due to C. Difficile infection.

- AbbVie: The event is exacerbation of underlying UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 116 U/L (normal 30 to 120)

[redacted] 20[redacted] ALT: 40 U/L (normal <45)

[redacted] 20[redacted] APTT: 30.3 SEC (normal 24.0 to 35.0)

[redacted] 20[redacted] AST: 21 U/L (normal <35)

[redacted] 20[redacted] Colonoscopy:

- severe disease (spontaneous bleeding, ulceration) in rectum and sigmoid

- Moderate disease (marked erythema, absent vascular pattern, friability, erosions) in descending colon, transverse colon and ascending colon/rectum

[redacted] 20[redacted] Colonoscopy:

- Moderate disease (marked erythema, absent vascular pattern, friability, erosions) in rectum and sigmoid

- Mild disease (erythema, decreased vascular pattern, and mild friability) in descending colon, transverse colon and ascending colon/rectum

[redacted] 20[redacted] CREATININE: 1.3 mg/dL (normal 0.8 to 1.2)

[redacted] 20[redacted] ECG: the normal range

Unknown date ENDOSCOPY: Not reported

[redacted] 20[redacted] Ferrum: 7 MCG/DL (normal 70 to 180)

[redacted] 20[redacted] GLUCOSE: 162 mg/dL (normal 74 to 106)

[redacted] 20[redacted] HEMOGLOBIN: 8.9 G/DL (normal 12.0 to 17.0)

[redacted] 20[redacted] High sensitivity C-reactive protein: 47.3 MG/L (normal 0 to 5)

[redacted] 20[redacted] POTASSIUM: 4.3 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] RECTOSCOPY: Colitis (Mayo 3)

[redacted] 20[redacted] SODIUM: 132 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] Toxin A and B of Clostridium difficile (stool): positive

[redacted] 20[redacted] X-RAY OF ABDOMEN: Enlarged intestinal loops were not seen; single levels of fluids were exposed inside intestinal loops

[redacted] 20[redacted] X-RAY OF CHEST: In the peripheral part of the center area of left lung, there is a slightly visible shadow (diameter 13mm) below front section IV rib.

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 EVERY WEEK	3[redacted]	MALE	White

Medical History	Onset Year
OTHER: INTOLERANCE PENICYLLIN	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 197	141

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]
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	4.5 g (gram(s))	QD	Y-M: 20[redacted]
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
BUDESONIDE	1 TABLET	QD	Y-M: 20[redacted] / -273
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -153
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -81
SUPREP BOWEL PREP	176 mL (millilitre(s))	QD	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4.5 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
HYDROCORTISONE	200 mg (milligram(s))	BID	Y-M: 20[redacted] / 200	Y-M: 20[redacted] / 203
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / 200	Y-M: 20[redacted] / 207
PERIKABIVEN	1540 mL (millilitre(s))	QD	Y-M: 20[redacted] / 201	Y-M: 20[redacted] / 203
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / 202	ONGOING
PREDNISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 207

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

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 200 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 200): HEMATOCRIT: 0.39 [0.4 - 0.54] FRACTION; HEMOGLOBIN: 131 [120 - 170] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 18.2 [5 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 201): Stool TEST FOR CLOSTRIDIUM DIFFICILE INFECTION: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 200): X-RAY ABDOMINAL: EXCLUDED MEGACOLONTOXICUM; [redacted]20[redacted] (RX DAY

201): RECTOSIGMOIDOSCOPY: MAYO 3	
AE Stopped Rx Day	207 (10 DAYS AFTER LAST TREATMENT)
Duration of AE	8 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	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（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，潰瘍性大腸炎（全大腸炎型）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，被験者は腹痛，発熱，及び血液が混じった下痢のため病院を受診した。身体的診察において腹部の圧痛が認められた。その後，同日に被験者は入院した。治療が実施され，被験者の体調は良くなり症状も消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治験責任医師により，被験者が本事象に関連するリスク因子を有しているかどうかは不明であると判断された。本事象の既往歴はなく，本事象に関連する家族歴もなかった。
治療薬として Pentasa（メサラジン），Corhydron，Asamax（メサラジン），Kabiven，Encorton，アザチオプリン，Eziclen，及び Vivomixx が投与された。

The patient's past medications include:

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

ENCORTON for ULCERATIVE COLITIS and COLITIS ULCEROSA ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted]

20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CORTIMENT MMX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PENICILLIN for UNKNOWN INDICATION

Causality for HUMIRA 40MG/0.8ML (Blinded)

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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: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

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

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: EXACERBATION OF ULCERATIVE COLITIS

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CLOSTRIDIUM DIFFICLE INFECTION: negative

[redacted] 20[redacted] HEMATOCRIT: 38.7 % (normal 40.0 to 54.0)

[redacted] 20[redacted] HEMOGLOBIN: 13.1 G/DL (normal 12.0 to 17.0)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 18.2 no units (normal 5.0 to 5.0)

[redacted] 20[redacted] RECTROSIGMOIDOSCOPY: MAYO 3

[redacted] 20[redacted] XRAY ABDOMINAL: excluded megacolontoxicum

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
線維腫症	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	FEMALE	White

Medical History	Onset Year
Not reported.	

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 59	[redacted]20[redacted] / 267	209

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] / -124
BUDESONIDE	9 g (gram(s))	QD	Y-M: 20[redacted] / -124
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -124
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -105
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -42
SUPREP BOWEL PREP	176 mL (millilitre(s))	QD	Y-M: 20[redacted] / -11

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -124	Y-M: 20[redacted] / 268
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / 269	Y-M: 20[redacted] / 273
METEOSPASMYL	1 CAPSULE	BID	Y-M: 20[redacted] / 269	Y-M: 20[redacted] / 273
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / 274	Y-M: 20[redacted] / 299
DIAZEPAM	UNK mg (milligram(s))	Other: UNK	Y-M: 20[redacted] / 297	Y-M: 20[redacted] / 297
MIDAZOLAM	UNK mg (milligram(s))	Other: UNK	Y-M: 20[redacted] / 297	Y-M: 20[redacted] / 297
DALTEPARIN	UNK mL (millilitre(s))	QD	Y-M: 20[redacted] / 300	Y-M: 20[redacted] / 304
PREDNISONE	45 mg (milligram(s))	QD	Y-M: 20[redacted] / 300	Y-M: 20[redacted] / 306
MESALAZINE	UNK g (gram(s))	Other: UNK	Y-M: 20[redacted] / 300	Y-M: 20[redacted] / 313
METRONIDAZOLE	UNK mg (milligram(s))	Other: UNK	Y-M: 20[redacted] / 300	Y-M: 20[redacted] / 313
SPEKTRAMOX	UNK mg (milligram(s))	Other: UNK	Y-M: 20[redacted] / 300	Y-M: 20[redacted] / 313
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 307	Y-M: 20[redacted] / 313
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / 314	ONGOING
PREDNISONE	35 mg (milligram(s))	QD	Y-M: 20[redacted] / 314	Y-M: 20[redacted] / 320

PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 327
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 328	Y-M: 20[redacted] / 334
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 335	Y-M: 20[redacted] / 341

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

Event Description	AGGRESSIVE FIBROMATOSIS
Preferred term	線維腫症
AE Onset Date / Rx Day	[redacted]20[redacted] / 182
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 270): CA 125: 94.2 [0 - 35] U/ML; CA 15-3: 20.5 [0 - 31.3] NO DATA; CA 19-9: 3.18 [0 - 37] U/ML; CEA: 1.56 [0 - 5] NG/ML; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 3.12 [0 - 5] MG/L; LDH: 124 [91 - 180] IU/L; [redacted]20[redacted] (RX DAY 271): CMV IGG: 0.70 [NOT REPORTED - 6] AU/ML; CMV IGM: 0.40 [NOT REPORTED - 0.85] AU/ML; EBNA: 0.16 [NOT REPORTED - 0.5] AU/ML; EBV IGG: 59.33 [NOT REPORTED - 0.75] AU/ML; EBV IGM: 0.11 [NOT REPORTED - 0.5] AU/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 270): ABDOMINAL USG,: ABDOMINAL USG, [redacted].20[redacted]_LYMPHADENOPATHY; [redacted]20[redacted] (RX DAY 271): VIDEO-DERMATOSCOPY: SKIN NODULES OF MODERATE INFLAMMATION. HISTOPATHOLOGY RESULT: DESMOID; [redacted]20[redacted] (RX DAY 275): ABDOMINAL CT: IN PELVIS MINOR NON-HOMOGENOUS LITHOCYSTIC INFILTRATION ON MESENTERY AND BILATERAL PARAMETRIUM 120X110X95MM; [redacted]20[redacted] (RX DAY 278): USG PELVIS: TUMOR SIZE 120X110X108; [redacted]20[redacted] (RX DAY 285): USG PELVIS: OVARIES BILATERAL ENLARGED: RIGHT 56X36 MM, LEFT: 66 X 45 MM; [redacted]20[redacted] (RX DAY 313): USG PELVIS: TUMOR SIZE 125X46X105; [redacted]20[redacted] (RX DAY 319): USG PLEURA CAVITIS: HYDROTHORAX; [redacted]20[redacted] (RX DAY 320): USG PELVIS: TUMOR SIZE 116X48X105; [redacted]20[redacted] (RX DAY 322): THORACOCENTESIS: NCS; CHEST X-RAY: NCS; [redacted]20[redacted] (RX DAY 324): USG PELVIS: OVARIES BILATERAL ENLARGED: RIGHT 94 X 51 MM, LEFT: 71 X 34 MM; [redacted]20[redacted] (RX DAY 341): USG PELVIS: TUMOR SIZE 113X38X115; [redacted]20[redacted] (RX DAY 369): USG PELVIS: TUMOR SIZES: 110X56X95 MM

AE Stopped Rx Day	273 (6 DAYS AFTER LAST TREATMENT)
Duration of AE	92 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	AGGRESSIVA FIBROMATOSIS - BENIGN TUMOR OF THE OVARY
Preferred term	線維腫症
AE Onset Date / Rx Day	[redacted]20[redacted] / 290 (23 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 291): CA125: 75.1 [0 - 35] U/ML; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.78 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 292): ECG: NORMAL; [redacted]20[redacted] (RX DAY 297): LAPAROSCOPY: ABDOMINAL CAVITY FULL OF TUMORS UP TO THE LEVEL OF NAVEL. TUMORS APPERANCE OF LARGE, PLAIN, WHITISH `GRAPE BUNCHES? (8-10CM) COMING FROM THE PELVIC MINOR. LEFT OVARY WITH ABOVE TUMORS. RIGHT OVARY NOT; [redacted]20[redacted] (RX DAY 305): HISTOPATOLOGICAL STUDY - FRAGMENT OF THE: WEAVING OF THE OVARY WITH STROMAL EDEMA

AE Stopped Rx Day	298 (31 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	AGGRESSIVE FIBROMATOSIS - A TUMOR IN THE SMALLER PELVIS
Preferred term	線維腫症
AE Onset Date / Rx Day	[redacted]20[redacted] / 300 (33 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 300): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 4.5 [NOT REPORTED - 5] MG/L; [redacted]20[redacted] (RX DAY 309): LDH: 152 [0 - 246] U/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 300): ABDOMINAL CT: N COMPARISON TO CT DATED [redacted]20[redacted]: -MORE FLUID IN PLEURAL CAVITIES; -PELVIC TUMOR SIZE 180MM (PREVIOUSLY 125MM). STRUCTURE IS SOLID, WELL-DEMARCATED, HIGHLY VASCULARIZED, TUMOR BORDERS ARE CHARACTE; CHEST X-RAY:

IAPHRAGMATIC RIBS - RIGHT FLUID, LEFT FREE; [redacted] (RX DAY 306): CHEST CT: RIGHT PLEURAL CAVITY-60MM FLUID. LEFT PLEURAL CAVITY-12MM FLUID. ENLARGED LYMPH NODES NOT NOTED. FREE FLUID AROUND LIVER AND SPLEEN.; [redacted] (RX DAY 311): THORACENTESIS: NO GROWTH OF BACTERIAL FLORA; [redacted] (RX DAY 312): OVARIAN BIOPSY_HISTOPATHOLOGY (SECOND RE: MICROSCOPIC VIEW DOES NOT GIVE BASE TO CONFIRM CANCER, IT IS RATHER BENIGN TUMOR OF OVARY. TWO POSSIBILITIES MAY BE TAKEN UNDER CONSIDERATION: MASSIVE OVARIAN EDEMA OR OVARIAN FIBROMATOSIS. OVARIAN FI

AE Stopped Rx Day	313 (46 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #4: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	A TUMOR IN THE SMALLER PELVIS (AGGRESSIVE FIBROMATOSIS)
Preferred term	線維腫症
AE Onset Date / Rx Day	[redacted] / 333 (66 DAYS AFTER LAST TREATMENT)
Age at AE Onset	[redacted]

Laboratory Testing

[redacted] (RX DAY 334): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.2 [NOT REPORTED - 5] MG/L

Microbiology

[redacted] (RX DAY 336): Other PLEURAL FLUID SEEDS: N

SAE Supplemental Procedure

[redacted] (RX DAY 333): CHEST X-RAY: IAPHRAGMATIC RIBS - RIGHT FLUID, LEFT FREE; [redacted] (RX DAY 334): CHEST X-RAY: NCS; [redacted] (RX DAY 336): THORACENTESIS: NO GROWTH OF BACTERIAL FLORA

AE Stopped Rx Day	337 (70 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] :02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の侵襲性線維腫，卵巣良性腫瘍（侵襲性線維腫），小骨盤腫瘍（侵襲性線維腫，20[redacted] 年 [redacted] 月 [redacted] 日発現），小骨盤腫瘍（侵襲性線維腫，20[redacted] 年 [redacted] 月 [redacted] 日発現），小骨盤腫瘍（侵襲性線維腫，20[redacted] 年 [redacted] 月 [redacted] 日発現），及び胸腔内水分貯留（侵襲性線維腫）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，侵襲性線維腫が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，卵巣良性腫瘍（侵襲性線維腫）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，卵巣良性腫瘍（侵襲性線維腫）は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，小骨盤腫瘍（侵襲性線維腫）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，小骨盤腫瘍（侵襲性線維腫）は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，小骨盤腫瘍（侵襲性線維腫）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，小骨盤腫瘍（侵襲性線維腫）は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，小骨盤腫瘍（侵襲性線維腫）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，小骨盤腫瘍（侵襲性線維腫）は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，胸腔内水分貯留（侵襲性線維腫）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，胸腔内水分貯留（侵襲性線維腫）は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，侵襲性線維腫は回復した。

20[redacted] 年 [redacted] 月より，播種性皮膚結節及びリンパ節症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，結節及びリンパ節腫大が認められ，被験者は入院した。腹腔の超音波検査，臨床検査，並びに皮膚変化部位のビデオ皮膚鏡検査及び生検が実施された。結果の報告はなかった。治験薬の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な容体で退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は卵巣良性腫瘍（侵襲性線維腫）のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日に実施された腹腔鏡検査の結果，腹腔に臍高まで至る腫瘍が認められた。子宮内の透明な遊離体液から生検用検体が 2 つ採取された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胃痛のため再入院した。コンピュータ断層撮影検査が実施され，腫瘍は卵巣由来である可能性が高いと判断された。卵巣腫瘍摘出術が実施された。病理組織学的検査の結果，線維腫症の疑いが認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は呼吸困難及び疲労のため救急治療室を受診し，数時間滞在した。胸腔穿刺，胸腔の超音波検査，及び胸部 X 線検査が実施された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は小骨盤腫瘍（侵襲性線維腫）及び腹痛のため再入院した。20[redacted] 年 [redacted] 月 [redacted] 日，胸腔穿刺が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，小骨盤腫瘍（侵襲性線維腫）の新たなエピソードが発現したため被験者は再入院した。20[redacted] 年 [redacted] 月 [redacted] 日に実施された血管造影術の結果，両方の胸腔に水分貯留が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸腔内水分貯留（侵襲性線維腫）のため再入院した。20[redacted] 年 [redacted] 月 [redacted] 日に実施された胸腔の超音波検査の結果，右胸腔内及び左胸腔内に遊離体液が認められた（それぞれ 47 mm 及び 17 mm）。採取した体液中に抗酸菌（マイコバクテリウム属）は検出されず，癌細胞は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，壁側胸膜のビデオ補助胸腔鏡下生検が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Auglavin，Meteospasmyl，ジアゼパム，ミダゾラム，ニトラゼパム，Clexane（エノキサパリンナトリウム），Fragmin（ダルテパリンナトリウム），Encorton，Pentasa（メサラジン），及びメトロニダゾールが投与された。

The patient's past medications include:

CORTIMENT MMX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Fibromatosis (10049444) (Fibromatosis (10049444)) [v.21.0] [10049444]

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

2) Fibromatosis (10049444) (Fibromatosis (10049444)) [v.21.0] [10049444]

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

3) Fibromatosis (10049444) (Fibromatosis (10049444)) [v.21.0] [10049444]

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

4) Fibromatosis (10049444) (Fibromatosis (10049444)) [v.21.0] [10049444]

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

5) Fibromatosis (10049444) (Fibromatosis (10049444)) [v.21.0] [10049444]

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

6) Pleural effusion (10035598) (Pleural effusion (10035598)) [v.21.0] [10035598]

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 AGGRESSIVE FIBROMATOSIS

- Investigator: Not applicable.

- AbbVie: Weak temporal association with less than 9 months study drug exposure prior to onset of the event. Event was more likely a pre-existing condition.

Event of AGGRESSIVA FIBROMATOSIS BENIGN TUMOR OF THE OVARY

- Investigator: Not applicable.

- AbbVie: Event more likely related to prior event of aggressive fibromatosis.

Event of AGGRESSIVE FIBROMATOSIS A TUMOR IN THE SMALLER PELVIS

- Investigator: Not applicable.

- AbbVie: Event more likely a complication of prior event of aggressive fibromatosis.

Event of A TUMOR IN THE SMALLER PELVIS (AGGRESSIVE FIBROMATOSIS)

- Investigator: Not applicable

- AbbVie: Event more likely a complication of prior event of aggressive fibromatosis.

Event of A TUMOR IN THE SMALLER PELVIS (AGGRESSIVE FIBROMATOSIS)

- Investigator: Not applicable

- AbbVie: Event more likely a complication of prior event of aggressive fibromatosis.

Event of AGGRESSIVE FIBROMATOSIS FLUID IN PLEURAL CAVITY

- Investigator: Not applicable.

- AbbVie: Event more likely a complication of prior event of aggressive fibromatosis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL CT: In pelvis minor non-homogenous lithocystic infiltration on mesentery and bilateral parametrium 120x110x95mm

[redacted] 20[redacted] ABDOMINAL CT: Pelvic tumor size 188mm

[redacted] 20[redacted] ABDOMINAL USG: Lymphadenopathy

[redacted] 20[redacted] ANGIOGRAPHY: fluid in both pleural cavaties

[redacted] 20[redacted] BRONCHOSCOPY: Normal

[redacted] 20[redacted] CA 125: 94.20 U/ML (normal 0 to 35)

[redacted] 20[redacted] CA 125: 75.1 U/ML (normal 0 to 35)

[redacted] 20[redacted] CA 15-3: 20.5 No units (normal 0 to 31.3)

[redacted] 20[redacted] CA 19-9: 3.18 U/ML (normal 0 to 37)

[redacted] 20[redacted] CEA: 1.56 NG/ML (normal 0 to 5)

[redacted] 20[redacted] CHEST X-RAY: diaphragmatic ribs - right fluid, left free

[redacted] 20[redacted] CHEST X-RAY: NCS

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

[redacted] 20[redacted] CHEST X-RAY: diaphragm angles free

[redacted] 20[redacted] CMV IGG: 0.70 AU/ML (normal <6.0)

[redacted] 20[redacted] CMV IGM: 0.40 AU/ML (normal 0.40 to 0.85)

[redacted] 20[redacted] EBNA: 0.16 AU/ML (normal <0.5)

[redacted] 20[redacted] EBV IGG: 59.33 No unit (normal <0.75)

[redacted] 20[redacted] EBV IGM: 0.11 No unit (normal <0.5)

[redacted] 20[redacted] ECG: normal

[redacted] 20[redacted] ECG: Sinus bradycardia 52/min. Uncharacteristic disorders of ventricles repolarization periods.

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 3.12 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.78 mg/l (normal 0 to 5.0)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 4.5 MG/L (normal 0 to 5.0)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.2 mg/L (normal <5.0)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 1.8 mg/L (normal <5.0)

[redacted] 20[redacted] HISTOPATOLOGICAL STUDY: Fragments of the pleura with focal small lymphocytic infiltration.

[redacted] 20[redacted] HISTOPATOLOGICAL STUDY - FRAGMENT OF THE PELVIC TUMOR: weaving of the ovary with stromal edema

[redacted] 20[redacted] LAPAROSCOPY: Abdominal cavity full of tumors up to the level of navel. Tumors appearance of large, plain, whitish ‘grape bunches’ (8-10cm) coming from the pelvic minor. Left ovary with above tumors. Right ovary not seen due to large, still tumors. Two biopsies collected. Free clear fluid in uterus. Sample collected.

[redacted] 20[redacted] LDH: 124 IU/L (normal 91 to 180)

[redacted] 20[redacted] NASAL SWAB: Methicillin-resistant staphylococcus aureus not grown.

[redacted] 20[redacted] PLEURAL FLUID: NO GROWTH OF FLORA

[redacted] 20[redacted] PLUERAL FLUID SEEDS (MICROBIOLOGY): negative

[redacted] 20[redacted] THORACENTESIS: No growth of bacterial flora

[redacted] 20[redacted] TCENTESIS: No growth of bacterial flora.

[redacted] 20[redacted] THORACENTESIS: No growth of bacterial flora.

[redacted] 20[redacted] TOTAL PROTEIN (CHEMISTRY): 6.24 G/DL (normal 6.60 to 8.70)

[redacted] 20[redacted] ULTRASOUND OF PLEURAL CAVITY: Free fluid in right pleural cavity (47mm) and left pleural cavity (17mm). Acid-fast mycobacteria not grown and cancer cells not found in collected fluid.

[redacted] 20[redacted] USG PELVIS: Tumor size 120x110x108

[redacted] 20[redacted] USG PELVIS: Tumor size 125x46x105

[redacted] 20[redacted] USG PELVIS: Tumor size 116x48x105

[redacted] 20[redacted] USG PELVIS: Tumor size 113x38x115

[redacted] 20[redacted] USG PELVIS: tumor sizes: 110x56x95 mm

[redacted] 20[redacted] USG PLEURA CAVITIS: Hydrothorax

[redacted] 20[redacted] VIDEO-DERMATOSCOPY: Skin nodules of moderate inflammation. Histopathology result: desmoid

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
肺炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	5[redacted]	MALE	White

Medical History	Onset Year
HYPERTENSION	20[redacted]
OTHER: DYSLIPIDEMIA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	18	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB 4040 MG MG EVERY WEEK		EW	[redacted]20[redacted] /	[redacted]20[redacted] / 115	58

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ATORVASTATIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]-04
RAMIPRIL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]-04
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]-05
AZATHIOPRINE	75 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / -265
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -189
FENTANYL	100 mcg (microgram(s))	QD	Y-M: 20[redacted]-[redacted] / -13
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -13
PICO-SALAX	1 SACHET	BID	Y-M: 20[redacted]-[redacted] / -13
PROPOFOL	100 mg (milligram(s))	QD	Y-M: 20[redacted]-[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
ATORVASTATIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted]	ONGOING
RAMIPRIL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted]	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / -265	ONGOING
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -189	Y-M: 20[redacted]-[redacted] / 110
KETOPROFEN	100 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 58	Y-M: 20[redacted]-[redacted] / 58
CEFTRIAXONE	1 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / 71	Y-M: 20[redacted]-[redacted] / 84
CLINDAMYCIN	600 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 71	Y-M: 20[redacted]-[redacted] / 84
ELECTROLYTES NOS	NOT REPORTED		Y-M: 20[redacted]-[redacted] / 71	Y-M: 20[redacted]-[redacted] / 84
ENOXAPARIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 71	Y-M: 20[redacted]-[redacted] / 84
GLUCOSE	NOT REPORTED		Y-M: 20[redacted]-[redacted] / 71	Y-M: 20[redacted]-[redacted] / 84
HYDROCORTISONE	100 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 71	Y-M: 20[redacted]-[redacted] / 84
LACTOBACILLUS ACIDOPHILUS	1 SACHET	QD	Y-M: 20[redacted]-[redacted] / 71	Y-M: 20[redacted]-[redacted] / 84

LEVOFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 84
MAGNESIUM SULFATE	NOT REPORTED		Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 84
MORPHINE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 84
PANTOPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 84
PARACETAMOL	NOT REPORTED		Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 84
SODIUM CHLORIDE	NOT REPORTED		Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 84
CEFTRIAXONE	1 g (gram(s))	BID	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
HYDROCORTISONE	100 mg (milligram(s))	BID	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
LEVOFLOXACIN	NOT REPORTED		Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
MAGNESIUM SULFATE	NOT REPORTED		Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
MORPHINE	NOT REPORTED		Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
NADROPARIN	NOT REPORTED		Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
PANTOPRAZOLE	NOT REPORTED		Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
PARACETAMOL	NOT REPORTED		Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
ROXITHROMYCIN	150 mg (milligram(s))	BID	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
SODIUM CHLORIDE	NOT REPORTED		Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
TORASEMIDE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 108
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 115
BUDESONIDE	9 mg (milligram(s))	Other: EVERY SECAND DAY	Y-M: 20[redacted] / 111	Y-M: 20[redacted] / 117
CEFOTAXIME	1 g (gram(s))	BID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129

CEFTRIAXONE	1 mg (milligram(s))	BID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
CIPROFLOXACIN	400 mg (milligram(s))	BID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
CLINDAMYCIN	300 mg (milligram(s))	BID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
ELECTROLYTES NOS	NOT REPORTED		Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
HYDROCORTISONE	100 mg (milligram(s))	BID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
LACTOBACILLUS ACIDOPHILUS	1 SACHET	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
MAGNESIUM SULFATE	NOT REPORTED		Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
MORPHINE	NOT REPORTED		Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
NADROPARIN	NOT REPORTED		Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
PANTOPRAZOLE	NOT REPORTED		Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
PARACETAMOL	NOT REPORTED		Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
ROXITHROMYCIN	150 mg (milligram(s))	BID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 129
BUDESONIDE	9 mg (milligram(s))	Other: EVERY THIRD DAY	Y-M: 20[redacted] / 118	Y-M: 20[redacted] / 124
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 135
CLINDAMYCIN	0.3 mg (milligram(s))	TID	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 136
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 137
PANTOPRAZOLE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / 134	ONGOING
DEXKETOPROFEN	NOT REPORTED		Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 140
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 140
NADROPARIN	NOT REPORTED		Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 140

OMEPRAZOLE	NOT REPORTED		Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 140
PREDNISONE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 140
BUDESONIDE	9 mg (milligram(s))	Other: EVERY SECOND DAY	Y-M: 20[redacted] / 138	Y-M: 20[redacted] / 145

Event #1: Serious Adverse Event

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 71
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 71): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 144.7 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 80): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 16.1 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 101): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 124.1 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 106): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 6 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 116): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 71.5 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 128): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 4.1 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 134): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 64.8 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 139): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 6.9 [0 - 5] MG/L

Microbiology

(RX DAY): Sputum MYCOBACTERIUM: N; [redacted]20[redacted] (RX DAY 71): Urine QUANTITATIVE URINE TEST: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA; Blood ANAEROBIC BACTERIA: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA; Blood AEROBIC BACTERIA: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA

SAE Supplemental Procedure

(RX DAY): CHEST X-RAY: OVER THE LEFT DIAPHRAGM, PATCHY SHADING, EXCEPT THAT THE PULMONARY FIELDS WITHOUT FOCAL LESIONS, RIGHT DIAPHRAGM SMOOTH, LEFT NOT VISIBLE, THE SILHOUETTE OF THE HEART APPROPRIATE; CHEST X-RAY: SLIGHT PROGRESSION OF CHANGES OVER THE LEFT DIAPHRAGM, PATCHY SHADING, EXCEPT THAT THE PULMONARY FIELDS WITHOUT FOCAL LESIONS, RIGHT DIAPHRAGM SMOOTH, LEFT NOT VISIBLE, THE SILHOUETTE OF THE HEART APP; OXYGEN THERAPY: THE PATIENT HAD DURING THE HOSPITALIZATION OXYGEN THERAPY; [redacted]20[redacted] (RX DAY 71): OXYGEN THERAPY: THE PATIENT HAD DURING THE HOSPITALIZATION OXYGEN THERAPY; TOMOGRAPHY: A SMALL AMOUNT OF FLUID IN THE PLEURAL CAVITIES, IN THE SEGMENT OF 9.10 LUNGS, UNEVEN COMPACTION THAT MAY CORRESPOND TO ATALECTATIC AND INFLAMMATORY LESIONS, BESIDES THE LUNGS WITHOUT FOCAL CHANGES; [redacted]20[redacted] (RX DAY 72): LUNG X-RAY: STREAKY AND MOTTLED SHADOWS OVER LEFT AND RIGHT DIAPHRAGM, PULMONARY FIELDS WITHOUT FOCAL LESIONS, VISIBLE DIAPHRAGMS; [redacted]20[redacted] (RX DAY 79): LUNG X-RAY: ALMOST COMPLETE REGRESSION OF FOCAL LESIONS; [redacted]20[redacted] (RX DAY 100): CHEST X-RAY: SHADING OVER THE LEFT DIAPHRAGM, IN ADDITION TO THE PULMONARY FIELDS WITHOUT FOCAL CHANGES, THE DIAPHRAGM SMOOTH, THE LEFT WRONGLY VISIBLE, THE SILHOUETTE OF THE HEART WIDENED; [redacted]20[redacted] (RX DAY 107): CHEST X -RAY: TOTAL REGRESSION OF CHANGES IN THE LOWER RIGHT FIELD; [redacted]20[redacted] (RX DAY 128): CHEST X-RAY: ALMOST COMPLETE REGRESSION OF CHANGES IN BOTH LOWER FIELDS, REST LIKE LAST TIME; [redacted]20[redacted] (RX DAY 134): CHEST X-RAY: PU

AE Stopped Rx Day	140 (25 DAYS AFTER LAST TREATMENT)
Duration of AE	70 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	PATIENT WAS ADMITTED TO THE HOSPITAL DUE TO CHEST PAIN,DYSPONOEA AND FEVER.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の肺炎が認められた。関連する病歴は，脂質異常症，高血圧，及び潰瘍性大腸炎であった。被験者は元喫煙者（1 日当たり 0.5 箱，喫煙期間 18 年）であり，断酒していた。

20[redacted] 年 [redacted] 月 [redacted] 日，肺炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は呼吸困難，左肩甲骨下の激痛，及び深呼吸のため入院した。被験者は肺炎と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。被験者は，20[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 日，20[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 日，及び 20[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 日に再入院した。

治療薬として Clexane（エノキサパリンナトリウム），Lakcid，硫酸マグネシウム，アセトアミノフェン，Tartriakson，Corhydron，Pranprazox，Diuver，Cipropol（シプロフロキサシン），Biotaksym（セフォタキシムナトリウム），Ceftriakson，Levoxa（レボフロキサシン），クリンダマイシン，0.9 %塩化ナトリウム溶液，5 %ブドウ糖溶液，PWE，Perfalgan，Controloc，Nolpaza，Fraxiparine，Dexak，Helicid（オメプラゾール），モルヒネ，Klimicin，Tavanic（レボフロキサシン），及び Rulid（ロキシスロマイシン）が投与された。

The patient's past medications include:

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

Causality for HUMIRA (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.21.1] [10035664]

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: Yes

Alternative Etiology for HUMIRA (Blinded)

Event of PNEUMONIA

- Investigator: The patient was admitted to the hospital due to chest pain, dyspnea and fever.

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] AEROBIC BACTERIA: Negative. no pathogen microorganism have been cultured from the collected material

[redacted] 20[redacted] ANAEROBIC BACTERIA: Negative. no pathogen microorganism have been cultured from the collected material

[redacted] 20[redacted] CHEST X-RAY: SHADING OVER THE LEFT DIAPHRAGM, IN ADDITION TO THE PULMONARY FIELDS WITHOUT FOCAL CHANGES, THE DIAPHRAGM SMOOTH, THE LEFT WRONGLY VISIBLE, THE SILHOUETTE OF THE HEART WIDENED

[redacted] 20[redacted] CHEST X-RAY: TOTAL REGRESSION OF CHANGES IN THE LOWER RIGHT FIELD

[redacted] 20[redacted] CHEST X-RAY: OVER THE LEFT DIAPHRAGM, PATCHY SHADING, EXCEPT THAT THE PULMONARY FIELDS WITHOUT FOCAL LESIONS, RIGHT DIAPHRAGM SMOOTH, LEFT NOT VISIBLE, THE SILHOUETTE OF THE HEART APPROPRIATE

[redacted] 20[redacted] CHEST X-RAY: SLIGHT PROGRESSION OF CHANGES OVER THE LEFT DIAPHRAGM, PATCHY SHADING, EXCEPT THAT THE PULMONARY FIELDS WITHOUT FOCAL LESIONS, RIGHT DIAPHRAGM SMOOTH, LEFT NOT VISIBLE, THE SILHOUETTE OF THE HEART APPROPRIATE

[redacted] 20[redacted] CHEST X-RAY: ALMOST COMPLETE REGRESSION OF CHANGES IN BOTH LOWER FIELDS, REST LIKE LAST TIME

[redacted] 20[redacted] CHEST X-RAY: PULMONARY FIELDS WITHOUT FOCAL LESIONS, RIGHT DIAPHRAGM SMOOTH, LEFT DIAGRAHM NOT VISIBLE WITH SHADED DIAPHRAGMATIC ANGLE, HEART SILHOUETTE IN NORMAL

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 144.7 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 16.1 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 124.1 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 6 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 71.5 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 4.1 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 64.8 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 6.9 MG/L (normal 0 to 5)

[redacted] 20[redacted] LUNG X-RAY: Streaky and mottled shadows over left and right diaphragm, pulmonary fields without focal lesions, visible diaphragms.

[redacted] 20[redacted] LUNG X-RAY: Almost complete regression of focal lesions

[redacted] 20[redacted] QUANTITATIVE URINE TEST: Negative. no pathogen microorganism have been cultured from the collected material

[redacted] 20[redacted] SPUTUM CULTURE: Mycobacterium negative

[redacted] 20[redacted] TOMOGRAPHY: A small amount of fluid in the pleural cavities, in the segment of 9.10 lungs, uneven compaction that may correspond to atelectomotor and inflammatory lesions, besides the lungs without focal changes

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			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	4[redacted]	MALE	White

Medical History	Onset Year
OTHER: ORCHITIS	20[redacted]
OTHER: THE PATIENT HAD HAD DIABETES VISIT AND THE DIABETOLOGIST DIAGNOSED DIABETES POST - STEROIDAL	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	9	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 280	224

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted]
CALCIUM	UNK mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted]
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg (milligram(s))	QID	Y-M: 20[redacted] / -286
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -68
METFORMIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / -19
SITAGLIPTIN	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
FENTANYL	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
PICO-SALAX	1 SACHET	BID	Y-M: 20[redacted] / -13
PROPOFOL	100 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
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
CALCIUM	UNK mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	1000 mg (milligram(s))	QID	Y-M: 20[redacted] / -286	ONGOING
GLICLAZIDE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 63	ONGOING
ELECTROLYTE SOLUTIONS	UNK mL (millilitre(s))	Other: UNK	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 126
IRON	100 mg (milligram(s))	BID	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 126
RED BLOOD CELLS	2 UNIT	QD	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 120
RED BLOOD CELLS	3 UNIT	QD	Y-M: 20[redacted] / 315	Y-M: 20[redacted] / 315
ELECTROLYTES NOS	UNK mL (millilitre(s))	Other: 3 TIMES PER DAY	Y-M: 20[redacted] / 318	Y-M: 20[redacted] / 320
METAMIZOLE	1000 mg (milligram(s))	PRN	Y-M: 20[redacted] / 326	ONGOING
NADROPARIN	0.3 ML	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] / 337

326

Event #1: Serious Adverse Event

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 119
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 120): HEMOGLOBIN: 78 [135 - 172] G/L; [redacted]20[redacted] (RX DAY 123): HEMOGLOBIN: 99 [135 - 172] G/L

Microbiology

(RX DAY): Stool SALMONELLA,SHIGELLA,YERSINIA: N; Stool CLOSTRIDIUM DIFFICILE: N

SAE Supplemental Procedure

(RX DAY): 2 UNITS OF PACKED (CONCENTRATED)RED BLO: 2 UNITS 0F PACKED(CONCENTRATED)RED BLOOD CELLS WERE TRANSFUSED TO THE PATIENT

AE Stopped Rx Day	126
Duration of AE	8 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	THE PATIENT WAS ADMITTED TO THE HOSPITAL DUE TO VERY LOW LEVEL OF HEMOGLOBIN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	EXACERBATION OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 288 (8 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 320): HEMOGLOBIN: 111 [131 - 172] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 315): COLECTOMY: TOTAL INTRA-ABDOMINAL COLECTOMY; 3 UNITS OF PACKED (CONCENTRATED)RED BLO: 3 UNITS OF PACKED (CONCENTRATED) RED BLOOD CELLS WERE TRANSFUSED TO THE PATIENT; [redacted]20[redacted] (RX DAY 321): X- RAY OF CHEST: PLEURAL CAVITIES WITHOUT FLUID, PULMONARY FIELDS WITHOUT VISIBLE PARENCHYMAL CONSTRICTIONS, VISIBLE GAS UNDER DIAPHRAGM DOMES - CONDITION AFTER SURGERY - TO BE CHECKED AT THE CONTROL VISIT

AE Stopped Rx Day	326 (46 DAYS AFTER LAST TREATMENT)
Duration of AE	39 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	THE PATIENT WAS ADMITTED TO THE HOSPITAL DUE TO COLON RESECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の貧血が認められた。関連する病歴は，潰瘍性大腸炎及びステロイド糖尿病であった。被験者は断酒していた。
20[redacted] 年 [redacted] 月 [redacted] 日，貧血が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，ヘモグロビン値が非常に低かったため被験者は入院した。被験者は，ステロイド依存性潰瘍性大腸炎の既往歴を有していた。20[redacted] 年 [redacted] 月 [redacted] 日，濃厚赤血球 2 単位分の輸血が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として PWE（生理食塩水），赤血球濃厚液，及び CosmoFer が投与された。

The patient's past medications include:

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

Causality for HUMIRA (Blinded)

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1) Anemia (10002272) (Anaemia (10002034)) [v.21.1] [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

Alternative Etiology for HUMIRA (Blinded)

Event of ANEMIA

- Investigator: THE PATIENT WAS ADMITTED TO THE HOSPITAL DUE TO VERY LOW LEVEL OF HEMOGLOBIN

- AbbVie: RISK FACTOR INCLUDES PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HAEMOGLOBIN: 7.8 G/DL (normal 13.3 to 17.2)

[redacted] 20[redacted] HAEMOGLOBIN: 9.9 G/DL (normal 13.3 to 17.2)

[redacted] 20[redacted] STOOL: Negative C. diff, Salmonella, Shigella, Yersinia
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（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，潰瘍性大腸炎及びステロイド糖尿病であった。被験者は元喫煙者（1 日当たり 0.5 箱，喫煙期間 9 年）であり，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，大量の血便が認められたことにより，生物学的療法による初期治療に奏効しなかったと判断されたため，被験者は入院した。結腸全摘術が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，濃厚赤血球 3 単位分の輸血が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

本事象により治験薬の投与は中止された。

治療薬として Pyralgina，赤血球濃厚液，及び Fraxiparine が投与された。

The patient's past medications include:

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

ENCORTON for ULCERATIVE COLITIS and REDUCTION OF DOSE ([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])

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

Causality for HUMIRA (Blinded)

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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: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of EXACERBATION OF UC

- Investigator: The patient was admitted to the hospital due to colon resection.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] 20[redacted] CHEST X-RAY: pleural cavities without fluid, pulmonary fields without visible parenchymal constrictions, visible gas under diaphragm domes - condition after surgery - to be checked at the control visit.

[redacted] 20[redacted] HEMOGLOBIN: 11.1 G/DL

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 EVERY WEEK	2[redacted]	FEMALE	White

Medical History	Onset Year
Not reported.	

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.4 PACKS	3	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 45	45
ADALIMUMAB 4040 MG MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 59	[redacted]20[redacted] / 358	300

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4000 mg (milligram(s))	QD	Y-M: 20[redacted]
PREDNISONE	40 g (gram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted]
MESALAZINE	500 g (gram(s))	QD	Y-M: 20[redacted]
DESOGESTREL	75 mcg (microgram(s))	QD	Y-M: 20[redacted] / -128
MESALAZINE	5000 g (gram(s))	QD	Y-M: 20[redacted] / -52
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -52
FENTANYL	100 mcg (microgram(s))	QD	Y-M: 20[redacted] / -19
MIDAZOLAM	2 mg (milligram(s))	QD	Y-M: 20[redacted] / -19
PICO-SALAX	1 SACHET	BID	Y-M: 20[redacted] / -19
PROPOFOL	60 mg (milligram(s))	QD	Y-M: 20[redacted] / -19

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	5000 g (gram(s))	QD	Y-M: 20[redacted] / -52	Y-M: 20[redacted] / 366
IRON	100 mg (milligram(s))	BID	Y-M: 20[redacted] / 207	Y-M: 20[redacted] / 211
PARACETAMOL	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 208
RED BLOOD CELLS	2 UNITS	QD	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 208
DROTAVERINE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 209
POTASSIUM	600 mg (milligram(s))	TID	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 209
MESALAZINE	3000 g (gram(s))	QD	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 395
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 392	ONGOING
RED BLOOD CELLS	1 UNITS	QD	Y-M: 20[redacted] / 392	Y-M: 20[redacted] / 392
DROTAVERINE	40 mg (milligram(s))	PRN	Y-M: 20[redacted] / 392	Y-M: 20[redacted] / 395
PARACETAMOL	1 g (gram(s))	PRN	Y-M: 20[redacted] / 392	Y-M: 20[redacted] / 395
SODIUM CHLORIDE	500 mL (millilitre(s))	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] / 395

			392	
RED BLOOD CELLS	1 UNITS	QD	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 393
RED BLOOD CELLS	1 UNITS	QD	Y-M: 20[redacted] / 394	Y-M: 20[redacted] / 394
RED BLOOD CELLS	1 UNITS	QD	Y-M: 20[redacted] / 395	Y-M: 20[redacted] / 395

Event #1: Serious Adverse Event

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 207
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 207): HEMOGLOBIN: 63 [120 - 154] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 30.7 [0 - 5] MG/L; POTASSIUM: 5 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 209): HEMOGLOBIN: 77 [120 - 154] G/L; [redacted]20[redacted] (RX DAY 210): HEMOGLOBIN: 93 [120 - 154] G/L; POTASSIUM: 3.7 [3.5 - 5.2] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 207): Stool SALMONELLA: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.; Stool ANTIGEN CLOSTRIDIUM DIFFICILE: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.; Stool NOROVIRUS: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.; Stool ADENOVIRUSES: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.; Stool ANIGEN GLUTAMATE DEHYDROGENASE: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.; Stool SHIGELLA: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.; Stool ANTIGEN ROTAVIRUS: N-NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.

SAE Supplemental Procedure

(RX DAY): 2 UNITS OF PACKED (CONCENTRATED) RED BL: 2 UNITS 0F PACKED(CONCENTRATED)RED BLOOD CELLS WERE TRANSFUSED TO THE PATIENT

AE Stopped Rx Day	211
Duration of AE	5 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	THE PATIENT WAS ADMITTED TO THE HOSPOITAL DUE TO LOW SCORE OF HGB
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	DEEP SYMPTOMATIC ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 390 (32 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 392): HEMATOCRIT: 0.24 [0.36 - 0.45] FRACTION; HEMOGLOBIN: 67 [120 - 154] G/L; IRON: 11 [37 - 145] ?G/DL; MCH: 18.6 [27 - 33.5] PG; MCHC: 27.7 [31.5 - 36] G/DL; MCV: 67 [80 - 99] FL; RED BLOOD COUNT: 3.6 [3.9 - 5.2] X10^12/L; [redacted]20[redacted] (RX DAY 395): HEMATOCRIT: 0.36 [0.36 - 0.45] FRACTION; HEMOGLOBIN: 111 [120 - 154] G/L; MCH: 22.9 [27 - 33.5] PG; MCHC: 30.7 [31.5 - 36] G/DL; MCV: 74.6 [80 - 99] FL; RED BLOOD COUNT: 4.8 [3.9 - 5.2] X10^12/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 392): 1 UNIT OF PACKED (CONCENTRATED) RED BLOO: 1 UNITS OF PACKED (CONCENTRATED) RED BLOOD CELLS WERE TRANSFUSED TO THE PATIENT.; [redacted]20[redacted] (RX DAY 393): 1 UNIT OF PACKED (CONCENTRATED) RED BLOO: 1 UNITS OF PACKED (CONCENTRATED) RED BLOOD CELLS WERE TRANSFUSED TO THE PATIENT; [redacted]20[redacted] (RX DAY 394): 1 UNIT OF PACKED (CONCENTRATED) RED BLOO: 1 UNITS OF PACKED (CONCENTRATED) RED BLOOD CELLS WERE TRANSFUSED TO THE PATIENT; [redacted]20[redacted] (RX DAY 395): 1 UNIT OF PACKED (CONCENTRATED) RED BLOO: 1 UNITS OF PACKED (CONCENTRATED) RED BLOOD CELLS WERE TRANSFUSED TO THE PATIENT

AE Stopped Rx Day	395 (37 DAYS AFTER LAST TREATMENT)
Duration of AE	6 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	THE PATIENT, AFTER UNSCHEDULED VISIT, WAS IMMEDIATELY REFERRED TO THE HOSPITAL BECAUSE OF THE DEPTH OF SYMPTOMATIC ANEMIA. THE INVESTIGATOR HAS BEEN INFORMED ABOUT ADVERSE EVENT ON [redacted] 20[redacted].
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の貧血が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。被験者は喫煙者（1 日当たり 0.4 箱，喫煙期間 3 年）であり，断酒していた。
20[redacted] 年 [redacted] 月 [redacted] 日，貧血が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な貧血が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な貧血は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，ヘモグロビン低値，脱力，及び連日の直腸出血のため被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として CosmoFer 及び濃厚赤血球（2 単位）が投与された。

The patient's past medications include:

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

Causality for HUMIRA (Blinded)

---

1) Anemia (10002272) (Anaemia (10002034)) [v.21.1] [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

Alternative Etiology for HUMIRA (Blinded)

Event of ANEMIA

- Investigator: THE PATIENT WAS ADMITTED TO THE HOSPOITAL DUE TO LOW SCORE OF HGB.

- AbbVie: RISK FACTOR INCLUDES PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ADENOVIRUSES: STOOL NEGATIVE: NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.

[redacted] 20[redacted] ANIGEN GLUTAMATE DEHYDROGENASE: STOOL NEGATIVE: NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.

[redacted] 20[redacted] ANTIGEN CLOSTRIDIUM DIFFICILE: STOOL NEGATIVE: NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.

[redacted] 20[redacted] ANTIGEN ROTAVIRUS: STOOL NEGATIVE: NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.

[redacted] 20[redacted] HEMOGLOBIN: 6.3 G/DL (normal 12.0 to 15.4)

[redacted] 20[redacted] HEMOGLOBIN: 7.7 G/DL (normal 12.0 to 15.4)

[redacted] 20[redacted] HEMOGLOBIN: 9.3 G/DL (normal 12.0 to 15.4)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 30.7 MG/L (normal 0 to 5)

[redacted] 20[redacted] NOROVIRUS: STOOL NEGATIVE: NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.

[redacted] 20[redacted] SHIGELLA: STOOL NEGATIVE: NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.

[redacted] 20[redacted] STOOL: SALMONELLA TEST NEGATIVE: NO PATHOGEN MICROORGANISM HAVE BEEN CULTURED FROM THE COLLECTED MATERIA.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の深在性症候性貧血が認められた。関連する病歴は，潰瘍性大腸炎であった。被験者は喫煙者（1 日当たり 0.4 箱，喫煙期間 3 年）であり，非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，深在性症候性貧血が認められた。

被験者は以前にも貧血が認められていた（20[redacted] 年 [redacted] 月 [redacted] 日発現）。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はヘモグロビン低値，脱力，及び連日の直腸出血が認められた（重度の症候性貧血）ため，予定外で病院を受診し，その後病院へ搬送された。20[redacted] 年 [redacted] 月 [redacted] 日，[redacted] 日，[redacted] 日，及び [redacted] 日にそれぞれ濃厚赤血球 1 単位分の輸血（合計 4 単位）が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師により，被験者は全ての治験薬投与を終了し，重篤な有害事象である本事象は追跡調査期間中に発現したと判断された。

治療薬として塩化ナトリウム及び濃厚赤血球が投与された。

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], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

NO-SPA for STOMACH ACH DUE TO EXACERBATION OF UC ([redacted] 20[redacted] - [redacted] 20[redacted])

RED BLOOD CELLS, CONCENTRATED for ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

---

1) Anemia (10002272) (Anaemia (10002034)) [v.22.0] [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 (Blinded)

Event of DEEP SYMPTOMATIC ANEMIA

- Investigator: Not reported

- AbbVie: Risk factor including pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HEMATOCRIT: 24.2 % (normal 35.5 to 45.0)

[redacted] 20[redacted] HEMATOCRIT: 36.1 % (normal 35.5 to 45.0)

[redacted] 20[redacted] HEMOGLOBIN: 7.7 G/DL (normal 12.0 to 15.4)

[redacted] 20[redacted] HEMOGLOBIN: 6.7 G/DL (normal 12.0 to 15.4)

[redacted] 20[redacted] HEMOGLOBIN: 11.1 G/DL (normal 12.0 to 15.4)

[redacted] 20[redacted] IRON: 11 MCG/DL (normal 37 to 145)

[redacted] 20[redacted] MCH: 18.6 PG (normal 27 to 33.5)

[redacted] 20[redacted] MCH: 22.9 PG (normal 27 to 33.5)

[redacted] 20[redacted] MCHC: 27.7 G/DL (normal 31.5 to 36)

[redacted] 20[redacted] MCHC: 30.7 G/DL (normal 31.5 to 36)

[redacted] 20[redacted] MCV: 67.0 FL (normal 80 to 95)

[redacted] 20[redacted] MCV: 74.6 FL (normal 80 to 95)

[redacted] 20[redacted] RBC: 3.61 T/L (normal 3.9 to 5.15)

[redacted] 20[redacted] RBC: 4.84 T/L (normal 3.9 to 5.15)

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
視神経萎縮	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	4[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: CESAREAN SECTION	19[redacted]
DEPRESSION: PATIENT SUFFERS FROM DEPRESSION. INFORMATION ADDED AFTER END OF HER PARTICIPATION IN THIS STUDY.	20[redacted]
OTHER: CONCUSSION	20[redacted]
OTHER: DIZZINESS	20[redacted]
OTHER: HEAD INJURY	20[redacted]
OTHER: LOST CONSCIOUSNESS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 99	43

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PAROXETINE	20 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted]
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted]-[redacted] / -160
AZATHIOPRINE	2 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / -128
PICO-SALAX	2 SACHETS	QD	Y-M: 20[redacted]-[redacted] / -16

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PAROXETINE	20 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted]	ONGOING
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted]-[redacted] / -160	ONGOING
METHYLPREDNISOLONE	UNK UNKNOWN	QD	Y-M: 20[redacted]-[redacted] / 105	Y-M: 20[redacted]-[redacted] / 112
PANTOPRAZOLE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted]-[redacted] / 105	Y-M: 20[redacted]-[redacted] / 112

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

Event Description	OTHER DISORDERS OF THE OPTIC NERVE (N. II) AND THE VISUAL PATH - ATROPHY OF THE OPTIC NERVE
Preferred term	視神経萎縮
AE Onset Date / Rx Day	[redacted]20[redacted] / 102 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 105): HEMATOCRIT: 0.38 [0.36 - 0.45] FRACTION; HEMOGLOBIN: 127 [120 - 154] G/L; PLATELET COUNT: 306 [140 - 440] X10^9/L; POTASSIUM: 4.7 [3.5 - 5.1] MMOL/L; RED BLOOD COUNT: 4.9 [3.9 - 5.2] X10^12/L; SODIUM: 137 [136 - 146] MMOL/L; WHITE BLOOD COUNT: 6.8 [3.9 - 10.2] X10^9/L; [redacted]20[redacted] (RX DAY 106): HEMATOCRIT: 0.35 [0.36 - 0.45] FRACTION; HEMOGLOBIN: 117 [120 - 154] G/L; LYME DISEASE

IGG: 12.2 [0 - 16] RU/ML; LYME DISEASE IGM: 13.1 [0 - 16] RU/ML; PLATELET COUNT: 284 [140 - 440] X10^9/L; POTASSIUM: 4.1 [3.5 - 5.1] MMOL/L; RED BLOOD COUNT: 4.5 [3.9 - 5.2] X10^12/L; SODIUM: 135 [136 - 146] MMOL/L; WHITE BLOOD COUNT: 6.1 [3.9 - 10.2] X10^9/L; [redacted]20[redacted] (RX DAY 107): CSF CHLORIDES: 132 H [115 - 130] MMOL/L; CSF GLUCOSE: 79 [50 - 80] MG/DL; CSF PROTEIN: 24 [15 - 45] MG/DL; LINK-TIBLING IGG: 11.32 [7 - 16] G/DL; LINK-TIBLING INDEX A: 3.78 [3.5 - 5.2] G/DL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 107): FLUID PUNCTURE - CEREBRAL SPINAL FLUID: RESULT IN NORMAL RANGE;
20[redacted] (RX DAY 112): MRI HEAD AND NECK: THERE IS NO EVIDENCE OF DEMYELINATING PROCESS.;
20[redacted] (RX DAY 189): OCT-RNFL: RIGHT EYE: NORMAL THICKNESS OF THE NERVE FIBER LAYER. LEFT EYE: DIFFUSED THINNING OF THE NERVE FIBER LAYER.; OCT OF THE MACULAS: RIGHT EYE: NORMAL MACULA MORPHOLOGY. LEFT EYE: VISIBLE THINNING OF THE RETINA IN THE MACULA.;
[redacted]20[redacted] (RX DAY 190): OD/OS VEP AND OD/OS FVEP TESTING.: PVEP OD - NORMAL SHAPE AND PARAMETERS OF THE RECORDING. OS - ABNORMAL WAVEFORM, LOW AMPLITUDE RECORDING, BORDERLINE P100 LATENCY. FVEP OD/OS - ASYMMETRICAL RECORDINGS, LOW AMPLITUDES OF P2 WAVES IN OS; [redacted]20[redacted](RX DAY 275): OCT OF MACULAS: RIGHT EYE: NORMAL MACULA MORPHOLOGY. LEFT EYE: VISIBLE THINNING OF THE RETINA IN THE MACULA.; OCT - RNFL: RIGHT EYE: NORMAL THICKNESS OF THE NERVE FIBER LAYER. LEFT EYE: DIFFUSED THINNING OF THE NERVE FIBER LAYER, STABLE CONDITION.

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の視神経（N. II）及び視覚経路の他の障害（視神経萎縮）が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。被験者は非喫煙者であり，元アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，視神経（N. II）及び視覚経路の他の障害（視神経萎縮）が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，左目の視力不足が認められて左目の球後視神経炎と初期診断され，被験者は入院した。その後，診断は確定された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として IPP 及び 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）が投与された。

Causality for HUMIRA (Blinded)

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1) Atrophy optic nerve (10003715) (Optic atrophy (10030910)) [v.21.1] [10003715]

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: No

Alternative Etiology for HUMIRA (Blinded)

Event of OTHER DISORDERS OF THE OPTIC NERVE (N. II) AND THE VISUAL PATH - ATROPHY OF THE OPTIC NERVE

- Investigator: Not applicable

- AbbVie: EVENT'S ETIOLOGY IS NOT CONSISTENT WITH STUDY DRUG'S MECHANISM OF ACTION.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CEREBRAL SPINAL FLUID ANALYSIS: RESULT IN NORMAL RANGE: Tibling index: ALBUMIN 9.5 L MG/DL, IGG 0.2 L MG/DL

[redacted] 20[redacted] CSF CHLORIDE: 132 MMOL/L (normal 115 to 130)

[redacted] 20[redacted] CSF GLUCOSE: 79 mg/dL (normal 50 to 80)

[redacted] 20[redacted] CSF PROTEIN: 24 mg/dL (normal 15 to 45)

[redacted] 20[redacted] HEMATOCRIT: 38.1 % (normal 35.5 to 45.0)

[redacted] 20[redacted] HEMATOCRIT: 34.8 % (normal 35.5 to 45.0)

[redacted] 20[redacted] HEMOGLOBIN: 12.7 G/DL (normal 12.0 to 15.4)

[redacted] 20[redacted] HEMOGLOBIN: 11.7 G/DL (normal 12.0 to 15.4)

[redacted] 20[redacted] LINK TIBLING IGG: 11.32 G/DL (normal 7.0 to 16.0)

[redacted] 20[redacted] LINK-TIBLING INDEX A: 3.78 G/DL (normal 3.5 to 5.2)

[redacted] 20[redacted] LYME DISEASE IGG: 12.2 RU/mL (normal 0 to 16)

[redacted] 20[redacted] LYME DISEASE IGM: 13.1 RU/mL (normal 0 to 16)

[redacted] 20[redacted] MRI HEAD AND NECK: THERE IS NO EVIDENCE OF DEMYELINATING PROCESS

[redacted] 20[redacted] OCT - RNFL: Right eye: normal thickness of the nerve fiber layer. Left eye: diffused thinning of the nerve fiber layer, stable condition.

[redacted] 20[redacted] OCT OF MACULAS: Right eye: normal macula morphology. Left eye: visible thinning of the retina in the macula.

[redacted] 20[redacted] OCT OF THE MACULAS: Right eye: normal macula morphology. Left eye: visible thinning of the retina in the macula.

[redacted] 20[redacted] OCT-RNFL: Right eye: normal thickness of the nerve fiber layer. Left eye: diffused thinning of the nerve fiber layer.

[redacted] 20[redacted] OD/OS VEP AND OD/OS FVEP TESTING: PVEP OD - normal shape and parameters of the recording. OS - abnormal waveform, low amplitude recording, borderline P100 latency. FVEP OD/OS - asymmetrical recordings, low amplitudes of P2 waves in OS.

[redacted] 20[redacted] PLATELET COUNT: 306 X10**3/MCL (normal 140 to 440)

[redacted] 20[redacted] PLATELET COUNT: 284 X10**3/MCL (normal 140 to 440)

[redacted] 20[redacted] POTASSIUM: 4.69 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] POTASSIUM: 4.1 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] RBC (HEMATOLOGY): 4.86 X10**6/MCL (normal 3.90 to 5.15)

[redacted] 20[redacted] RBC (HEMATOLOGY): 4.48 X10**6/MCL (normal 3.90 to 5.15)

[redacted] 20[redacted] SODIUM: 137 MMOL/L (normal 136 to 146)

[redacted] 20[redacted] SODIUM: 135 MMOL/L (normal 136 to 146)

[redacted] 20[redacted] WBC (HEMATOLOGY): 6.80 X10**3/MCL (normal 3.9 to 10.2)

[redacted] 20[redacted] WBC (HEMATOLOGY): 6.10 X10**3/MCL (normal 3.9 to 10.2)

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
ADALIMUMAB 40 MG EVERY OTHER WEEK	1[redacted]	MALE	White

Medical History	Onset Year
SURGERY: LEFT ORCHIDOPEXY UNDER GENERAL SURGERY	19[redacted]
ASTHMA: MILD ASTHMA	20[redacted]
SURGERY: RIGHT DISTAL TIBIAL FRACTURE	20[redacted]
SURGERY: REMOVAL OF DCP PLATE FROM THE RIGHT TIBIA	20[redacted]
SURGERY: REDUCTION NASAL BONES CLOSED	20[redacted]
ATRIAL FIBRILLATION/ATRIAL FLUTTER: PAROXYSMAL ATRIAL FIBRILATION	20[redacted]
ANEMIA: IRON DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 28	28
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 59	[redacted]20[redacted] / 124	66

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MERCAPTOPURINE	50 mg (milligram(s))	Other: ONDE DAILY	Y-M: 20[redacted]
BISOPROLOL	125 mg (milligram(s))	QD	Y-M: 20[redacted]
CICLOSPORIN	150 mg (milligram(s))	BID	Y-M: 20[redacted]
FLECAINIDE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -244
PREDNISOLONE	20 mg (milligram(s))	Other: ONCE DAILY	Y-M: 20[redacted] / -210
ALLOPURINOL	100 mg (milligram(s))	Other: ONCE DAILY	Y-M: 20[redacted] / -168
AZATHIOPRINE	25 mg (milligram(s))	Other: ONCE DAILY	Y-M: 20[redacted] / -168
MEBEVERINE	135 mg (milligram(s))	TID	Y-M: 20[redacted] / -154
LEKOVIT CA	400 IU (international unit(s))	Other: 1 TABLET TWICE DAILY	Y-M: 20[redacted] / -112
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted] / -76
HYOSCINE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -47
MIDAZOLAM	4 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -47
PETHIDINE	50 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -47
SODIUM PICOSULFATE	1 APPLICATION	Other: ONCE	Y-M: 20[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
MEBEVERINE	135 mg (milligram(s))	TID	Y-M: 20[redacted] -154	/ONGOING

LEKOVIT CA	400 IU (international unit(s))	Other: 1 TABLET TWICE DAILY	Y-M: 20[redacted] /ONGOING -112
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted] /ONGOING -76
EL-4	0.9% + 0.15% % (percent)	QID	Y-M: 20[redacted] /Y-M: 20[redacted] / 140 141
DALTEPARIN	5000 IU (international unit(s))	QD	Y-M: 20[redacted] /Y-M: 20[redacted] / 140 146
PREDNISOLONE	40 mg (milligram(s))	BID	Y-M: 20[redacted] /Y-M: 20[redacted] / 140 147
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] /Y-M: 20[redacted] / 140 147
PARACETAMOL	1000 mg (milligram(s))	PRN	Y-M: 20[redacted] /ONGOING 141
MORPHINE	2.5 mg (milligram(s))	PRN	Y-M: 20[redacted] /Y-M: 20[redacted] / 141 141
INFLIXIMAB	315 mg (milligram(s))	Other: ONCE ONLY	Y-M: 20[redacted] /Y-M: 20[redacted] / 141 142
MEBEVERINE	135 mg (milligram(s))	TID	Y-M: 20[redacted] /ONGOING 142
OMEPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] /ONGOING 142
HYDROCORTISONE	100 mg (milligram(s))	Other: ONCE ONLY	Y-M: 20[redacted] /Y-M: 20[redacted] / 142 142
INFLIXIMAB	315 mg (milligram(s))	Other: MONTHLY	Y-M: 20[redacted] /Y-M: 20[redacted] / 142 142
CHLORPHENAMINE	4 mg (milligram(s))	Other: TWO DOSES ONLY ON [redacted] AND [redacted]	Y-M: 20[redacted] /Y-M: 20[redacted] / 142 147
CODEINE	30-60 mg (milligram(s))	QID	Y-M: 20[redacted] /Y-M: 20[redacted] / 142 147
VEDOLIZUMAB	300 mg (milligram(s))	Other: ONCE ONLY	Y-M: 20[redacted] /ONGOING 146

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] / 132 (8 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 140): ALANINE AMINO TRANSFERASE (SGPT/ALT): 9 [0 - 50] U/L; ALBUMIN: 37 [35 - 50] G/L; ALKALINE PHOSPHATASE: 71 [38 - 126] U/L; CREATININE: 77 [64 - 104] MCMOL/L; HEMATOCRIT: 0 [0 - 0.01] FRACTION; HEMOGLOBIN: 126 [130 - 170] G/L; PLATELET COUNT: 367 [150 - 410] X10^9/L; POTASSIUM:

3.8 [3.6 - 5] MMOL/L; RED BLOOD COUNT: 4.7 [4.5 - 5.5] X10^12/L; SODIUM: 138 [134 - 145] MMOL/L; TOTAL BILIRUBIN: 4 [0 - 22] MCMOL/L; WHITE BLOOD COUNT: 4.2 [4 - 10] X10^9/L

Microbiology

[redacted] 20[redacted] (RX DAY 140): Other NOSE AND GROIN SWABS BACTERIAL SCREENING: N; Stool CL DIFFICILE: N; [redacted] 20[redacted] (RX DAY 141): Stool BACTERIOLOGY: N

SAE Supplemental Procedure

[redacted] 20[redacted] (RX DAY 141): FLEXIBLE SIGMOIDOSCOPY: MODERATELY ACTIVE COLITIS; ECG: NORMAL SINUS RHYTHM

AE Stopped Rx Day	147 (23 DAYS AFTER LAST TREATMENT)
Duration of AE	16 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	LACK OF EFFICACY OF STUDY DRUG
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted] :02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，1[redacted] 歳の男性（英国）であり，重篤な有害事象の潰瘍性大腸炎再燃が認められた。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，潰瘍性大腸炎再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃のため被験者は入院した。静脈内輸液及びステロイド投与による治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，軟性 S 状結腸鏡検査が実施された結果，中等度の活動性大腸炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてプレドニゾロン，生理食塩水，カリウム，ダルテパリン，mebeverine，オメプラゾール，Inflectra（インフリキシマブ），chlorphenamine，ベドリズマブ，アセトアミノフェン，ヒドロコルチゾン，コデインリン酸塩水和物，Oramorph，及びインフリキシマブが投与された。

The patient's past medications include:

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

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

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

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

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

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

Causality for HUMIRA (Open Label)

---

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: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of FLARE OF ULCERATIVE COLITIS

- Investigator: Lack of efficacy of study drug

- AbbVie: The event is exacerbation of underlying disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] creatinine: 77 mg/dl

[redacted] 20[redacted] hemoglobin: 126 G/DL (normal 130 to 170)

[redacted] 20[redacted] sigmoidoscopy: moderate active colitis

[redacted] 20[redacted] stool culture: negative for Cl difficile

[redacted] 20[redacted] WBC: 4.2 X10**9/L (normal 4.0 to 10.0)

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
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	6[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: RIGHT HEMITHYROIDECTOMY	20[redacted]
OTHER: LUMP IN RIGHT BREAST FOLLOWING TRAUMA	20[redacted]
OTHER: PROCTITIS	20[redacted]
OTHER: MILD OSTEOPENIA OF THE LEFT FEMORAL NECK	20[redacted]
OTHER: MODERATE OSTEOPENIA OF LUMBAR SPINE	20[redacted]
OTHER: IRON DEFICIENCY ANAEMIA	NOT REPORTED
OTHER: POST MENOPAUSAL	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0 PACKS	1	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2-4 drinks per day

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 55	[redacted]20[redacted] / 357	303

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -267
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -257
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -217
PREDNISOLONE	30 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -184
BUDESONIDE	2 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -174
MESALAZINE	400 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / -140
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -57

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	400 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / -140	ONGOING
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 70	Y-M: 20[redacted]-[redacted] / 141
LEKOVIT CA	1 TABLET	BID	Y-M: 20[redacted]-[redacted] / 140	ONGOING
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / 142	ONGOING
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 142	Y-M: 20[redacted]-[redacted] / 156

Event #1: Serious Adverse Event

Event Description	FLARE OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 139
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 139): ALANINE AMINO TRANSFERASE (SGPT/ALT): 8 [0 - 50] U/L; ALBUMIN: 24 [35 - 50] G/L; ALKALINE PHOSPHATASE: 84 [38 - 126] U/L; CALCIUM: 2.19 [2.1 - 2.6] MMOL/L; CREATININE: 53 [49 - 90]

MCMOL/L; HEMATOCRIT: 0 [0 - 0] FRACTION; HEMOGLOBIN: 123 [120 - 150] G/L; PLATELET COUNT: 691 [150 - 410] X10^9/L; POTASSIUM: 3.6 [3.6 - 5] MMOL/L; RED BLOOD COUNT: 4.6 [3.8 - 4.8] X10^12/L; SODIUM: 131 [134 - 149] MMOL/L; TOTAL BILIRUBIN: 6 [0 - 22] MCMOL/L; TOTAL PROTEIN: 57 [63 - 82] G/L; WHITE BLOOD COUNT: 12.1 [4 - 10] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 139): Stool C DIFF: N; [redacted]20[redacted] (RX DAY 140): Stool NOROVIRUS RNA: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 140): ABDOMEN X-RAY: NORMAL; [redacted]20[redacted] (RX DAY 142): FLEXIBLE SIGMOIDOSCOPY: MINIMAL RECTAL AND SIGMOID GRANULARITY - LEFT SIDED COLITIS DID NOT LOOK VERY ACTIVE　IMPRESSION THAT CURRENT BRIEF UPSET MAY HAVE BEEN INFECTIVE

AE Stopped Rx Day	142
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	POSSIBLE INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の女性（英国）であり，重篤な有害事象の潰瘍性大腸炎再燃が認められた。関連する病歴は，直腸炎，左側潰瘍性大腸炎，鉄欠乏性貧血であった。被験者はアルコール摂取者（1 日当たり 2～4 ドリンク）であった。

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

20[redacted] 年 [redacted] 月 [redacted] 日，突然の下痢及び嘔吐が認められ，被験者は入院した。また，被験者の 2 人の孫及び義理の娘に過去 2 週間にわたって下痢及び嘔吐が認められていた。入院時の 1 日当たりの排便頻度は 10 回であり，血液が混じった下痢であった。入院以降，排便頻度は 1 日当たり 2 回に落ち着いた。入院中に症状は改善し，被験者が退院する際にはプレドニゾロン投与量が減量された。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，ランソプラゾール，ダルテパリン，プレドニゾロン，及び Adcal D3 が投与された。

The patient's past medications include:

PREDNISOLONE for ULCERATIVE COLITIS and FLARE OF ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

Causality for HUMIRA (Blinded)

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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 (Blinded)

Event of FLARE OF UC

- Investigator: Possible infection

- AbbVie: The event is exacerbation of underlying disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Abdomen x-ray: normal

[redacted] 20[redacted] C Diff: Negative

[redacted] 20[redacted] Flexible sigmoidoscopy:

Minimal rectal and sigmoid granularity – left sided colitis did not look very active. Impression that current brief upset may have been infective.

[redacted] 20[redacted] Norovirus RNA: Negative

[redacted] 20[redacted] Platelet count: 691 X10**9/L (normal 150 to 410)

[redacted] 20[redacted] Sodium: 131 MMOL/L (normal 134 to 149)

[redacted] 20[redacted] total protein: 57 G/L (normal 63 to 82)

[redacted] 20[redacted] WBC: 12.1 X10**9/L (normal 4.0 to 10.0)

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
類天疱瘡	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	3[redacted]	MALE	White

Medical History	Onset Year
OTHER: ULCERATIVE COLITIS	20[redacted]
OTHER: BLISTERS ON BOTH INNER THIGHS (1 ON EACH SIDE) AND 1 ON LEFT LEG	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	2	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB TDM	40/40 MG	EOW/EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 148	92

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	225 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted]
HYOSCINE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -9
SODIUM PICOSULFATE	1 APPLICATION	Other: ONCE	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
AZATHIOPRINE	225 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
AMOXICILLIN	500 mg (milligram(s))	QID	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 138
AUGMENTIN	500/125 mg (milligram(s))	TID	Y-M: 20[redacted] / 138	Y-M: 20[redacted] / 145
DERMOL	500 IU (international unit(s))	QID	Y-M: 20[redacted] / 140	ONGOING
FUCICORT	0.1 % (percent)	QD	Y-M: 20[redacted] / 140	ONGOING

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

Event Description	BULLOUS PEMPHIGOID ON BOTH LEGS, ARMS AND ABDOMEN
Preferred term	類天疱瘡
AE Onset Date / Rx Day	[redacted]20[redacted] / 118
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	148
Duration of AE	31 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　IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（英国）であり，重篤な有害事象の両足，両腕，及び腹部における水疱性類天疱瘡が認められた。関連する病歴は，両大腿部内側の水疱であった。
20[redacted] 年 [redacted] 月 [redacted] 日，両足，両腕，及び腹部における水疱性類天疱瘡が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，両足，両腕，及び腹部における水疱性類天疱瘡は回復した。
両足，腹部，及び両腕の皮膚に水疱が認められた。本事象は 1 ヵ月後に回復した。
治療薬として Dermol skin wash，Co-amoxiclav，アモキシシリン，Fucibet 及びプレドニゾロンが投与された。

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1)　Bullous pemphigoid (10006567)　(Pemphigoid (10034277))　[v.20.0]　[10006567]

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

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of BULLOUS PEMPHIGOID ON BOTH LEGS, ARMS AND ABDOMEN

- Investigator: N/A

- 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
上腹部痛	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	MALE	White

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
PERIPHERAL ARTHROPATHY: N/A	20[redacted]
OTHER: ANAL POLYP	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 45	45
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 60	[redacted]20[redacted] / 354	295

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 mg (milligram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 ng (nanogram(s))	TID	Y-M: 20[redacted] / -316
BECLOMETASONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -273
ALLOPURINOL	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -256
LEKOVIT CA	CALCIUM CARBONATE 1.5GRAM / 400 UNITS COLECALCIFEROL GRAMS / UNITS	BID	Y-M: 20[redacted] / -256
MERCAPTOPURINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -256
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -189
HYOSCINE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -15
MIDAZOLAM	2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -15
PETHIDINE	50 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -15
SODIUM PICOSULFATE	10 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -15

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4.8 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
LEKOVIT CA	CALCIUM CARBONATE 1.5GRAM / 400 UNITS COLECALCIFEROL GRAMS / UNITS	BID	Y-M: 20[redacted] / -256	ONGOING
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -189	ONGOING
MORPHINE	10 mg (milligram(s))	QID	Y-M: 20[redacted] / 322	Y-M: 20[redacted] / 330

Event #1: Serious Adverse Event

Event Description	UPPER RIGHT SIDE TRANSVERSE ABDOMINAL PAIN
Preferred term	上腹部痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 320

Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	323
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（英国）であり，重篤な有害事象の右上側腹部の疼痛が認められた。関連する病歴は，潰瘍性大腸炎であった。被験者はアルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，右上側腹部の疼痛が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，右上側腹部の疼痛は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。右側腹部の疼痛を含む兆候及び症状が認められた。潰瘍性大腸炎再燃と推察された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師により，被験者の本事象に関連するリスク因子及び家族歴は不明であると判断された。

治療薬として Oramorph が投与された。

The patient's past medications include:

AZATHIOPRINE for UC ([redacted] 20[redacted] - [redacted] 20[redacted])

BECLOMETASONE DIPROPIONATE for UC ([redacted] 20[redacted] - [redacted] 20[redacted])

ALLOPURINOL for UC ([redacted] 20[redacted] - [redacted] 20[redacted])

MERCAPTOPURINE for UC ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for HUMIRA (Blinded)

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1) Right upper quadrant pain (10039162) (Abdominal pain upper (10000087)) [v.21.0] [10039162]

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 UPPER RIGHT SIDE TRANSVERSE ABDOMINAL PAIN

- Investigator: N/A

- 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
好中球数減少	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	4[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: PENICILLIN DRUG ALLERGY	19[redacted]
OTHER: INTERSTITIAL CYSTITIS	20[redacted]
OTHER: KIDNEY STONES	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 60	[redacted]20[redacted] / 113	54

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MOVIPREP	2 SACHETS	Other: ACCORDING TO INSTRUCTIONS	Y-M: 20[redacted] / -15

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
CLOTRIMAZOLE	1 CAPSULE OF 150MG FLUCONAZOLE ONCE ONLY USED WITH VAGINAL 150MG FLUCONAZOLE AND 2% CLOTRIMAAZOLE	Other: 1 CAPSULE OF 150MG FLUCONAZOLE ONE OFF DOSE - USED WITH EXTERNAL VAGINAL CREAM - CLOTRIMAZOLE	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 119
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 123
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 124	ONGOING
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 124	ONGOING

Event #1: Serious Adverse Event

Event Description	LOW NEUTROPHILS
Preferred term	好中球数減少
AE Onset Date / Rx Day	[redacted]20[redacted] / 114 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 79): HEMOGLOBIN: 94 [120 - 160] G/L; WHITE BLOOD COUNT: 3.1 [4 - 11] X10^9/L;
[redacted]20[redacted] (RX DAY 85): HEMOGLOBIN: 101 [120 - 160] G/L; WHITE BLOOD COUNT: 3.3 [4 - 11] X10^9/L;
[redacted]20[redacted] (RX DAY 106): HEMOGLOBIN: 105 [120 - 160] G/L; WHITE BLOOD COUNT: 2.9 [4 - 11] X10^9/L;
[redacted]20[redacted] (RX DAY 113): HEMOGLOBIN: 107 [120 - 160] G/L; WHITE BLOOD COUNT: 3 [4 - 11] X10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING

Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	AE CHANGED TO A SAE ON [redacted]/20[redacted] PI DECISION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（英国）であり，重篤な有害事象の好中球数低値が認められた。関連する病歴は潰瘍性大腸炎であった。
被験者は以前（20[redacted] 年 [redacted] 月）に，低用量アザチオプリンによる治療時に白血球減少症が認められていた。
20[redacted] 年 [redacted] 月 [redacted] 日，好中球数低値が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な潰瘍性大腸炎再燃が認められ，軽度の好中球減少症も発現していた（治験薬の投与 2 週時）。好中球減少症は投与 16 週時まで継続した。残念ながら，疾患及び好中球減少症は悪化し，試験の中止及び治療法の変更が必要となった。治療薬としてオメプラゾール，プレドニゾロン，及びブデソニドが投与された。

Causality for HUMIRA (Blinded)

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1) Neutrophil count low (10029369) (Neutrophil count decreased (10029366)) [v.22.0] [10029369]

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

Alternative Etiology for HUMIRA (Blinded)

Event of LOW NEUTROPHILS

- Investigator: AE changed to a SAE ON [redacted] 20[redacted], investigator decision.

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HEMOGLOBIN: 94 G/L

[redacted] 20[redacted] HEMOGLOBIN: 101 G/L

[redacted] 20[redacted] HEMOGLOBIN: 105 G/L (normal 120 to 160)

[redacted] 20[redacted] HEMOGLOBIN: 107 G/L (normal 120 to 160)

[redacted] 20[redacted] NEUTROPHILS: 0.91 X10**9/L

[redacted] 20[redacted] NEUTROPHILS: 1.51 X10**9/L

[redacted] 20[redacted] NEUTROPHILS: 1.13 X10**9/L

[redacted] 20[redacted] NEUTROPHILS: 0.96 X10**9/L (normal 2.0 to 7.7)

[redacted] 20[redacted] WBC: 3.1 X10**9/L

[redacted] 20[redacted] WBC: 3.3 X10**9/L

[redacted] 20[redacted] WBC: 2.9 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] WBC: 3.0 X10**9/L (normal 4.0 to 11.0)

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
半月板損傷	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	6[redacted]	MALE	White

Medical History	Onset Year
BENIGN PROSTATIC HYPERPLASIA: ENLARGED PROSTATE, CORTICAL THINNING	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	UNKNOWN			
CIGARETTES	FORMER	0.5 PACKS	40	20[redacted]
CIGARS	UNKNOWN			
PIPES	UNKNOWN			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 29	29
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 362	305

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 mg (milligram(s))	Other: ONCE A DAY	Y-M: 20[redacted]
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted]
NUROFEN PLUS	4 TABLETS	QD	Y-M: 20[redacted] / -40
LEKOVIT CA	300 mg (milligram(s))	QD	Y-M: 20[redacted] / -35
PREDNISOLONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -35
MAGNESIUM CITRATE	UNKNOWN 2 X SACHETS	Other: TWICE	Y-M: 20[redacted] / -30
SENNA ALEXANDRINA	10 TABLETS TABLETS	Other: JUST ONCE	Y-M: 20[redacted] / -30

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4.8 mg (milligram(s))	Other: ONCE A DAY	Y-M: 20[redacted]	ONGOING
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
NUROFEN PLUS	4 TABLETS	QD	Y-M: 20[redacted] / -40	ONGOING
LEKOVIT CA	300 mg (milligram(s))	QD	Y-M: 20[redacted] / -35	ONGOING
AMLODIPINE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 260	ONGOING

Event #1: Serious Adverse Event

Event Description	MEDIAL MENISCAL TEAR IN LEFT KNEE
Preferred term	半月板損傷
AE Onset Date / Rx Day	[redacted]20[redacted] / 297
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 297): ARTHROSCOPY LEFT KNEE: RESOLVED

AE Stopped Rx Day	297
Duration of AE	1 DAY
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NONE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（英国）であり，重篤な有害事象の左膝内側半月板断裂が認められた。関連する病歴は，左側潰瘍性大腸炎であった。被験者は元喫煙者（1 日当たり 0.5 箱，喫煙期間 40 年）であった。
20[redacted] 年 [redacted] 月 [redacted] 日，左膝内側半月板断裂が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，左膝内側半月板断裂は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，左膝の疼痛が認められ，被験者は入院した。左膝の待機的関節鏡検査が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

PREDNISOLONE for TO PREVENT EXACERBATION OF UC SYMPTOMS, TO PREVENT EXACERBATION OF UC SYMPTOMS and ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CO-CODAMOL for LEFT LEG PAIN ([redacted] 20[redacted] - [redacted] 20[redacted])

Amitryptyline for LEFT LEG PAIN ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Meniscus tear of knee (10027291) (Meniscus injury (10072970)) [v.22.0] [10027291]

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 MEDIAL MENISCAL TEAR IN LEFT KNEE

- Investigator: Not reported

- AbbVie: Event's etiology is commonly associated with trauma.

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
ADALIMUMAB 40 MG EVERY OTHER WEEK	2[redacted]	MALE	White

Medical History	Onset Year
ASTHMA	20[redacted]
OTHER: JOINT STIFFNESS AND BODY ACHES	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 4040 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 60	[redacted]20[redacted] / 288	229

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	1 g (gram(s))	PRN	Y-M: 20[redacted]
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1 ENEMA	QD	Y-M: 20[redacted] / -219
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -69
PREDNISOLONE	1 ENEMA	QD	Y-M: 20[redacted] / -69

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	1 g (gram(s))	PRN	Y-M: 20[redacted]	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	50000 UNITS	Other: MONTHLY	Y-M: 20[redacted] / 139	ONGOING
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 204	ONGOING
MERCAPTOPURINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 251	ONGOING
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 285	Y-M: 20[redacted] / 291
PREDNISOLONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 292	Y-M: 20[redacted] / 298
DALTEPARIN	5000 UNITS	QD	Y-M: 20[redacted] / 318	Y-M: 20[redacted] / 330
CODEINE	30 mg (milligram(s))	PRN	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 330
METOCLOPRAMIDE	10 mg (milligram(s))	TID	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 330
CALCIUM CARBONATE	10 mL (millilitre(s))	QID	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 330
PARACETAMOL	1000 mg (milligram(s))	QID	Y-M: 20[redacted] / 325	Y-M: 20[redacted] / 330
SODIUM CHLORIDE	1000 mL (millilitre(s))	PRN	Y-M: 20[redacted] / 325	Y-M: 20[redacted] / 330
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 326	Y-M: 20[redacted] / 330

Event #1: Serious Adverse Event

Event Description	ONGOING UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 316 (28 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 317): PROCTOCOLECTOMY WITH FORMATION OF J POUC: AS ABOVE

AE Stopped Rx Day	327 (39 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HOSPITALIZATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（英国）であり，重篤な有害事象の進行中潰瘍性大腸炎が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，進行中潰瘍性大腸炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，進行中潰瘍性大腸炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日より非重篤な大腸炎再燃が認められ，20[redacted] 年 [redacted] 月 [redacted] 日に回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，直腸結腸切除術のため，被験者は待機的に入院した。進行中の活動性潰瘍性大腸炎の兆候及び症状が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，直腸結腸切除術が実施され，J 型回

腸瘻が造設された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。被験者は診断時より一定期間の間，活動性大腸炎が認められていた。

被験者は本事象に関連するリスク因子を有しておらず，本事象に関連する家族歴は不明であった。

治療薬としてアセトアミノフェン，ダルテパリン，codeine，炭酸カルシウム，0.9 %塩化ナトリウム溶液，メトロニダゾール，メトクロプラミド，及び Co-amoxiclav が投与された。

The patient's past medications include:

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

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

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

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Ulcerative colitis (10045365) (Colitis ulcerative (10009900)) [v.20.1] [10045365]

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 ONGOING UC

- Investigator: Hospitalization.

- AbbVie: Elective surgery related to 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
大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	2[redacted]	FEMALE	White

Medical History	Onset Year
ASTHMA	20[redacted]
OTHER: RIGHT KNEE ARTHROSCOPY AND MENISECTOMY	20[redacted]
OTHER: EAR INFECTION	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 28	28
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 71	15

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] / -127
MESALAZINE	2.4 g (gram(s))	QD	Y-M: 20[redacted] / -127
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -127
ETONOGESTREL	68 mg (milligram(s))	Other: IMPLANT	Y-M: 20[redacted] / -63
FLUCLOXACILLIN	250 mg (milligram(s))	QID	Y-M: 20[redacted] / -28
BUDESONIDE	9 mg (milligram(s))	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
MESALAZINE	2.4 g (gram(s))	QD	Y-M: 20[redacted] / -127	ONGOING
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -127	Y-M: 20[redacted] / 85
ETONOGESTREL	68 mg (milligram(s))	Other: IMPLANT	Y-M: 20[redacted] / -63	ONGOING
BUDESONIDE	6 mg (milligram(s))	QD	Y-M: 20[redacted] / 28	ONGOING
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / 57	ONGOING
CODEINE	30 mg (milligram(s))	PRN	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 117
CLOBETASONE	0.05% g (gram(s))	PRN	Y-M: 20[redacted] / 60	ONGOING
EPADERM	NOT REPORTED	PRN	Y-M: 20[redacted] / 60	ONGOING
FUCICORT	NOT REPORTED	TID	Y-M: 20[redacted] / 60	ONGOING
LYMECYCLINE	408 mg (milligram(s))	QD	Y-M: 20[redacted] / 60	ONGOING

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

Event Description	ACUTE SEVERE COLITIS
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 76 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 76): ALBUMIN: 31 [32 - 50] G/L; HEMOGLOBIN: 137 [120 - 150] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 140.9 [0 - 5] MG/L; PLATELET COUNT: 350 [150 - 400] X10^9/L; WHITE BLOOD COUNT: 12.5 [4 - 11] X10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 81): LAPARASCOPIC SUBTOTAL COLECTOMY WITH ILE: UNCOMPLLICATED

RECOVERY DISCHARGED HOME	[redacted]
AE Stopped Rx Day	87 (16 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	DETERIORATION OF UC LEADING TO COLECTOMY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（英国）であり，重篤な有害事象の重度の急性大腸炎が認められた。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，重度の急性大腸炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，重度の急性大腸炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，下痢の悪化（1 日当たり 10 回を超え，全てに血液が混じっていた）が認められ，被験者は入院した。被験者の腹部は柔軟であったが，蒼白であった。頻脈（脈拍数 120 bpm）が認められ，体温は 37.7℃ であった。下痢，頻脈，悪心，体調不良，嗜眠，微熱，及び C 反応性たん白値の上昇を含む兆候及び症状が認められた。ステロイド剤の静脈内投与による治療が実施され，大腸の外科的処置が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，腹腔鏡下結腸亜全摘術及び回腸瘻造設が実施され，合併症は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として codeine が投与された。

The patient's past medications include:

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

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Colitis aggravated (10009890) (Colitis (10009887)) [v.20.1] [10009890]

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 40MG/0.8ML (Blinded)

Event of ACUTE SEVERE COLITIS

- Investigator: Deterioration of UC leading to colectomy

- AbbVie: The event is exacerbation of underlying disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Albumin: 31 G/L (normal 32 to 50)

[redacted] 20[redacted] Flexible sigmoidoscopy:

Rectum/Sigmoid = 3=severe disease(spontaneous bleeding, ulceration), presence of friability = yes, subscore=3

[redacted] 20[redacted] Flexible sigmoidoscopy:

Rectum/Sigmoid/Descending colon = 3 severe disease (spontaneous bleeding, ulceration), presence of friability = yes, subscore = 3

[redacted] 20[redacted] High-sensitivity c-reactive protein: 140.9 MG/L (normal 0 to 5)

[redacted] 20[redacted] Neutrophils: 8.70 X10**9/L (normal 2 to 7)

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
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	MALE	White

Medical History	Onset Year
OTHER: GASTRODUODENITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 4040 MG MG EVERY WEEK		EW	[redacted]20[redacted] / 59	[redacted]20[redacted] / 268	210

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] / -90
CIPROFLOXACIN	0 mg (milligram(s))	Other: UNK	Y-M: 20[redacted] / -90
MESALAZINE	0.8 g (gram(s))	Other: 5 TIMES PER DAY	Y-M: 20[redacted] / -90
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -90
METHYLPREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -90
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -27
METHYLPREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -27
METRONIDAZOLE	750 mg (milligram(s))	QD	Y-M: 20[redacted] / -27
PICO-SALAX	2 SACHETS	QD	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	0.8 g (gram(s))	Other: 5 TIMES PER DAY	Y-M: 20[redacted] / -90	ONGOING
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -90	Y-M: 20[redacted] / 296
METHYLPREDNISOLONE	24 mg (milligram(s))	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 260
DECAMETHOXINE	1 TABLET	QID	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 259
INTERFERON ALFA-2B	10 gtt (drop(s))	QID	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 259
AMBROXOL	30 mg (milligram(s))	TID	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 260
METHYLPREDNISOLONE	32 mg (milligram(s))	QD	Y-M: 20[redacted] / 261	Y-M: 20[redacted] / 269
BUDESONIDE	2 mg (milligram(s))	QD	Y-M: 20[redacted] / 270	ONGOING
BUDESONIDE	3 mg (milligram(s))	TID	Y-M: 20[redacted] / 270	ONGOING
METHYLPREDNISOLONE	24 mg (milligram(s))	QD	Y-M: 20[redacted] / 270	Y-M: 20[redacted] / 283
METHYLPREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 284	Y-M: 20[redacted] / 290
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] / 291	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] /	ONGOING

297

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 270 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 273): ECG: INCOMPLETE RIGHT BUNDLE BRANCH BLOCK;[redacted]20[redacted] (RX DAY 274): GASTROSCOPY: GASTRITIS; [redacted]20[redacted] (RX DAY 1370): ENDOSCOPY: ULCERATIVE COLITIS, PANCOLITIS MAYO 3	
AE Stopped Rx Day	297 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	28 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	INEFFICIENCY OF IMP TREATMENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（ウクライナ）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，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）及び胃十二指腸炎であった。

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，被験者は肛門科に入院した。重篤な有害事象である本事象の兆候及び症状として，貧血及び潰瘍性大腸炎の増悪が認められた。症状は治療により改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。リスク因子の可能性があるものとして外科手術が挙げられた。
治療薬として Metipred，Budenofalk，及び Imuran（アザチオプリン）が投与された。

The patient's past medications include:

CIPRINOL for UC ACTIVITY ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

Causality for HUMIRA (Blinded)

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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: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of EXACERBATION OF UC

- Investigator: INEFFICIENCY OF IMP TREATMENT

- AbbVie: THE EVENT IS EXACERBATION OF UNDERLYING UC.

Relevant Laboratory & Other Diagnostic Tests

Rectum/Sigmoid - 3 = Severity disease (spontaneous bleeding, ulceration); with presence of friability; Subscore 3

Rectum/Sigmoid/Descending colon: 3 = Severity disease (spontaneous bleeding, ulceration); with presence of friability; Subscore 3

[redacted] 20[redacted] ECG: Incomplete Right Bundle Branch Block

[redacted] 20[redacted] ENDOSCOPY: Ulcerative colitis, pancolitis Mayo 3

[redacted] 20[redacted] GASTROSCOPY: Gastritis

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
虚血性脳卒中	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	5[redacted]	MALE	White

Medical History	Onset Year
CHOLELITHIASIS	20[redacted]
LIVER DISEASE (EXCLUDING HEPATITIS): HEPATIC STEATOSIS	20[redacted]
OTHER: CHRONIC BRONCHITIS	20[redacted]
PANCREATITIS: CHRONIC PANCREATITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	FORMER			
CIGARETTES	FORMER	0.5 PACKS	23	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB TDM	40/40/160/40/160/40 MG	EOW/EW/EW/EW/EW/EW	[redacted]20[redacted] / 53	[redacted]20[redacted] / 358	306

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted] / -346
ARGININE GLUTAMATE	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -31
BUDESONIDE	3 mg (milligram(s))	TID	Y-M: 20[redacted] / -31
HALIBORANGE	1.0 mL (millilitre(s))	QD	Y-M: 20[redacted] / -31
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -31
PICO-SALAX	2 SACHET	QD	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
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted] / -346	ONGOING
BISOPROLOL	5 mg (milligram(s))	TID	Y-M: 20[redacted] / 362	ONGOING
VALSARTAN	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 362	ONGOING
ARGININE GLUTAMATE	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / 362	Y-M: 20[redacted] / 370
LYSINE	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / 362	Y-M: 20[redacted] / 370
TROPHICARD	1 TABLET	TID	Y-M: 20[redacted] / 362	Y-M: 20[redacted] / 381

Event #1: Serious Adverse Event

Event Description	ISCHEMIC STROKE
Preferred term	虚血性脳卒中
AE Onset Date / Rx Day	[redacted]20[redacted] / 362 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 365): HEMOGLOBIN: 125 [110 - 160] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 363): MAGNETIC RESONANCE IMAGING: ACUTE DISTURBANCE OF CEREBRAL CIRCULATION BY ISCHEMIC TYPE IN VERTEBRO-BASILAR BASIN; MAGNETIC RESONANCE IMAGING: DISCIRCULATORY ENCEPHALOPATHY; OPHTHALMOLOGIST EXAMINATION: DISC OF THE OPTIC NERVE: BLURRED BOUNDARIES ON THE RIGHT, ARTERIES NARROWED, VEINS DILATED; [redacted]20[redacted] (RX DAY 365): ULTRASONIC DOPPLER: STENOSIS OF THE CAROTID ARTERIES

AE Stopped Rx Day	381 (23 DAYS AFTER LAST TREATMENT)
Duration of AE	20 DAYS
Severity	Severe

Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UNKNOWN BY THE MOMENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（ウクライナ）であり，重篤な有害事象の虚血性脳卒中が認められた。関連する病歴は，潰瘍性大腸炎，慢性膵炎，及び脂肪肝であった。被験者は元喫煙者（1 日当たり 0.5 箱，喫煙期間 23 年）／元噛みたばこ使用者であり，元アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，虚血性脳卒中が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，虚血性脳卒中は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は仕事中に体調不良となり，回転性めまい，頭痛，及び言語障害が認められた。その後，被験者は自身の筆跡が変化していることに気づき，血圧は 170/100 mmHg に上昇していた。被験者は救急車で病院に搬送されて入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Glutargin 40%，Vassar，L-Lysine Aescinat，Asparcam，及び Concor が投与された。

The patient's past medications include:

BUDENOFALK for ULCERATIVE COLITIS ([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) Ischemic stroke (10055221) (Ischaemic stroke (10061256)) [v.20.1] [10055221]

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 (Blinded)

Event of ISCHEMIC STROKE

- Investigator: UNKNOWN AT THE MOMENT.

- AbbVie: RISK FACTORS INCLUDE PATIENT'S AGE, 2[redacted] YEARS OF SMOKING HISTORY AND PRE-EXISTING CHRONIC BRONCHITI

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] MAGNETIC RESONANCE IMAGING: ACUTE DISTURBANCE OF CEREBRAL CIRCULATION BY ISCHEMIC TYPE IN VERTEBRO-BASILAR BASIN

[redacted] 20[redacted] MAGNETIC RESONANCE IMAGING: Discirculatory encephalopathy

[redacted] 20[redacted] OPHTHALMOLOGIST EXAMINATION: DISC OF THE OPTIC NERVE: BLURRED BOUNDARIES ON THE RIGHT, ARTERIES NARROWED, VEINS DILATED

[redacted] 20[redacted] ULTRASONIC DOPPLER: STENOSIS OF THE CAROTID ARTERIES

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			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	5[redacted]	MALE	White

Medical History	Onset Year
NEPHROLITHIASIS	20[redacted]
ANEMIA: SECONDARY ANEMIA	20[redacted]
PANCREATITIS: CHRONIC	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB TDM	40/40/160/40/160/40 MG	EOW/EW/EW/EW/EW/EW	[redacted]20[redacted] / 55	[redacted]20[redacted] / 357	303

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1000 mg (milligram(s))	QID	Y-M: 20[redacted] / -55
PREDNISOLONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -55
MOVIPREP	200 g (gram(s))	Other: TO DILUTE WITH 2 L OF WATER & TO TAKE 200 ML EVERY 15 MIN FROM 15:00 TILL 19:00	Y-M: 20[redacted] / -4

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1000 mg (milligram(s))	QID	Y-M: 20[redacted] / -55	ONGOING
VENSY	230 mg (milligram(s))	TID	Y-M: 20[redacted] / 175	ONGOING
AMINOPHYLLINE	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 181
ASCORBIC ACID	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 181
CEFTRIAXONE	1 g (gram(s))	QD	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 181
CEFTRIAXONE	2 g (gram(s))	QD	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 181
DECAMETHOXINE	5 mL (millilitre(s))	QD	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 181
REOSORBILACT	200 mL (millilitre(s))	QD	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 181
SALBUTAMOL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 181

Event #1: Serious Adverse Event

Event Description	ACUTE BRONCHITIS
Preferred term	気管支炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 170
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	

Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	181
Duration of AE	12 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	COMMON COLD
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（ウクライナ）であり，重篤な有害事象の急性気管支炎が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，急性気管支炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，急性気管支炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，急性気管支炎（咳嗽及び 5 日間続く発熱）が認められ，被験者は入院した。重篤な有害事象である本事象の兆候及び症状は，咳嗽，発熱（38.7°C），脱力，及び胸痛であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Eufilin，PulmoBREATHE，Salbutamol，acidum ascorbinicum，decamethoxine，セフトリアキソン，及び Rheosorbilact が投与された。

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Acute bronchitis (10000687) (Bronchitis (10006451)) [v.19.1] [10000687]

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 40MG/0.8ML (Open Label)

Event of ACUTE BRONCHITIS

- Investigator: Common cold.

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] COLONOSCOPY: Rectum, Sigmoid, Descending colon- severe disease and Transverse colon, Ascending colon/cecum- moderate disease

[redacted] 20[redacted] COLONOSCOPY: Rectum, Sigmoid, Descending colon, Transverse colon- moderate disease, Ascending colon/cecum- mild disease

[redacted] 20[redacted] ELECTROCARDIOGRAM: Normal

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		
リンパ節症	X			
胸腔内リンパ節結核	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	6[redacted]	MALE	White

Medical History	Onset Year
OTHER: GASTRODUODENITIS	20[redacted]
PANCREATITIS: CHRONIC PANCREATITIS	20[redacted]
OTHER: CHRONIC PROSTATITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40	40 MG	EW	[redacted]20[redacted] /	[redacted]20[redacted] /	22

MG EVERY WEEK		57	78

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	800 mg (milligram(s))	TID	Y-M: 20[redacted] / -306
PREDNISOLONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -289
ISONIAZID	100 mg (milligram(s))	TID	Y-M: 20[redacted] / -83
RIFAMPICIN	150 mg (milligram(s))	QID	Y-M: 20[redacted] / -83
MACROGOL	200 g (gram(s))	Other: TO DILUTE WITH2L OF WATER AND TO TAKE 100 ML EV 15 MIN FROM 15 P.M. TO 19 P.M.	Y-M: 20[redacted] / -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	800 mg (milligram(s))	TID	Y-M: 20[redacted] / -306	ONGOING
PREDNISOLONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 53
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 61
PREDNISOLONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 76
CEFTRIAXONE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 81
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 81
TAMSULOSIN	0.4 mg (milligram(s))	QD	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 83
REOSORBILACT	200 mL (millilitre(s))	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 85
DEXAMETHASONE	8 mg (milligram(s))	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 87
FLUCONAZOLE	100 mL (millilitre(s))	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 88
CEFEPIME	1 g (gram(s))	BID	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 91
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 91
PROBIOTICS	460 mg (milligram(s))	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 116
CHLOROPYRAMINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 90
MEGLUMINE SODIUM SUCCINATE	200 mL (millilitre(s))	QD	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 88
FLUCONAZOLE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 92

DEXAMETHASONE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / 88 Y-M: 20[redacted] / 116
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 90 Y-M: 20[redacted] / 116
PREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 94 Y-M: 20[redacted] / 481

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

Event Description	UC EXACERBATION.
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 82 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 86): Sputum SPUTUM CULTURE+ ANTIBIOTIC SENSITIVITY: P-[redacted]20[redacted] - RESULT:STAPHYLOCOCCUS HEMOLYTICUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 82): SPIRAL COMPUTERTOMOGRAPHIE: HYPERSENSITIVE PNEUMONITIS; [redacted]20[redacted] (RX DAY 85): ULTRASOUND OF ABDOMINAL CAVITY & KIDNEYS: HEPATOMEGALIA,SPLENOMEGALIA, CHRONIC CHOLECYSTITIS,SYNDROME OF HYPOECHOIC SPLEEN FORMATIONS OF UNK ORIGIN; [redacted]20[redacted] (RX DAY 89): US OF HEART: WITHOUT ECHOPATHOLOGY EJECTION FRACTION 67%; [redacted]20[redacted] (RX DAY 98): CT SCAN: MEDIASTINAL AND BRONCHOPULMONARY BILATERAL LYMPHADENOPATHY; CT SCAN: SIGNS OF MULTIPLE SPLEEN FORMATIONS (SARCOIDOSIS?MILIARY FOCAL CHANGES OF BOTH LUNGS; [redacted]20[redacted] (RX DAY 100): MRI OF THE HEAD: DISCIRCULATORY ENCEPHALOPATHY, MILD EXTERNAL HYDROCEPHALUS; [redacted]20[redacted] (RX DAY 107): BRONCHOSCOPY: SIGNIFICANT DYSTROPHIC CHANGES IN THE MUCOSA OF BRONCHES & TRACHEA; [redacted]20[redacted] (RX DAY 113): CT SCAN: EXPRESSED INTRATHORACIC LYMPHADENOPATHY (MALIGNANT LYMPHOMA?), FOCAL DISSEMINATION IN THE LUNGS AND SPLEEN. BULLOUS EMPHYSEMA OF THE LUNG. HEPATOSPLENOMEGALY. THE FORMATION OF THE LEFT ADRENAL GLAND I

AE Stopped Rx Day	116 (38 DAYS AFTER LAST TREATMENT)
Duration of AE	35 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #2: Serious Adverse Event

Event Description	LYMPHADENOPATHY OF UNKNOWN ORIGIN OF THORACIC CAVITY
Preferred term	リンパ節症
AE Onset Date / Rx Day	[redacted]20[redacted] / 116 (38 DAYS AFTER LAST TREATMENT)

Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 119): MEDIASTINOSCOPY, BIOPSY OF PARATRACHEAL: IN PARATRACHEAL LYMPH NODES THE PHENOTYPE OF THE PROCESS CORRESPONDS TO FOCI OF CASEOUS NECROSIS WITH THE PRESENCE OF ACID-FAST MYCOBACTERIA, WITHOUT A SPECIFIC GRANULATING SHAFT, IN THE PHASE OF COMP	
AE Stopped Rx Day	147 (69 DAYS AFTER LAST TREATMENT)
Duration of AE	32 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Event #3: Serious Adverse Event

Event Description	TUBERCULOSIS OF THE INTRATHORACIC LYMPH NODES
Preferred term	胸腔内リンパ節結核
AE Onset Date / Rx Day	[redacted]20[redacted] / 148 (70 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 148): HIV TEST: NEGATIVE [NOT REPORTED - NOT REPORTED] OTHER; [redacted]20[redacted] (RX DAY 149): ABS.NEUTROPHILS: 2 [1.8 - 7] X10^9/L; HEMOGLOBIN: 1383 [132 - 170] G/L; RBC IN URINE: 1-2 [0 - 2] CELLS PER FIELD; RBC SEDEMENTATION: 30 [3 - 18] MM/HR; RED BLOOD COUNT: 4.2 [4.2 - 5.8] X10^12/L; RPR (RAPID PLASMA RE: NEG [NOT REPORTED - NOT REPORTED] OTHER; URINE GLUCOSE: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; URINE PROTEIN (DIPSTICK TEST): 0.041 [0 - 0.033] G/L; URINE SPECIFIC GRAVITY: 1.02 [1.01 - 1.022] N/A; WBC: 2-3 [1 - 3] CELLS PER FIELD; WHITE BLOOD COUNT: 5.1 [3.5 - 11.1] X10^9/L; [redacted]20[redacted] (RX DAY 378): ALANINE AMINO TRANSFERASE (SGPT/ALT): 42 [20 - 55] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 16 [5 - 34] U/L; BUN: 17 [3 - 9.2] MMOL/L; CREATININE: 202 [64 - 104] MCMOL/L; THYMOL TEST: 2.4 [0 - 4] UNITS; TOTAL BILIRUBIN: 34 [1 - 21] MCMOL/L; TOTAL PROTEIN: 63 [64 - 83] G/L	
Microbiology	
[redacted]20[redacted] (RX DAY 151): Sputum TB IDENTIFICATION: P-MICOBACTERIUM TUB. "+"; RIF "-", HSZ "+"	

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 149): X-RAY: BIG AREA OF THE INFILTARATION IN THE SAX ON RIGHT WITH THE FEW DECAY SECTORS (MAX 2,5 CM). MEDIUM INTENSITY FICIS ON THE REST OF THE BOTH SIDES. MEDIASTINUM IS EXTENDED IN THE THORACIC CAVITY DUE TO I; [redacted]20[redacted] (RX DAY 214): X-RAY: POSITIVE DINAMICS (NO OTHER DESCRIPTION AVAILABLE); [redacted]20[redacted] (RX DAY 245): X-RAY: POSITIVE DINAMICS (NO OTHER DESCRIPTION AVAILABLE); [redacted]20[redacted] (RX DAY 365): X-RAY: POSITIVE DINAMICS (NO OTHER DESCRIPTION AVAILABLE)

AE Stopped Rx Day	382 (304 DAYS AFTER LAST TREATMENT)
Duration of AE	235 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	AT THE START OF EVENT THERE WAS A SUSPICION TUBERCULOSIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（ウクライナ）であり，重篤な有害事象の胸腔内リンパ節結核，原因不明の胸腔リンパ節症，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，慢性膵炎，及び胃十二指腸炎であった。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，原因不明の胸腔リンパ節症が認められた。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，原因不明の胸腔リンパ節症は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，胸腔内リンパ節結核が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日より，発熱（38.5℃），下腹部重感，戦慄，及び軽度の咳嗽が認められていた。20[redacted] 年 [redacted] 月 [redacted] 日，発熱及び戦慄が断続的に認められたため，被験者は入院した。被験者の皮膚は湿っており，蒼白であった。肺に乾性喘鳴がわずかに認められ，血圧は 110/70 mmHg，脈拍は 60 bpm であったが，腹部は柔軟で疼痛はなかった。排便頻度は 1 日当たり 3～4 回であ

った。20[redacted] 年 [redacted] 月 [redacted] 日，コンピュータ断層撮影検査が実施された結果，縦隔及び両側気管支肺リンパ節症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，気管支鏡検査が実施された結果，両側気管支及び気管の粘膜に重大なジストロフィー変化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，原因不明の胸腔リンパ節症のため，被験者は胸部腫瘍科に転送された。20[redacted] 年 [redacted] 月 [redacted] 日，縦隔鏡検査及び気管傍リンパ節生検が実施された結果，壊死が認められ，抗酸菌（マイコバクテリウム属）が検出された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸部腫瘍科から退院した。20[redacted] 年 [redacted] 月 [redacted] 日，X 線検査結果にて結核の所見が確認され，臨床経過により，被験者は結核科に入院して右肺の結核治療を受けた。被験者は試験を中止した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬としてレボフロキサシン，Cebopimi，Dexamethasoni，Rheosorbilact，fluconazolum，プレドニゾロン，Kontroloc，Reamberin，Lactiale，Suprastinum，シプロフロキサシン，及び Omnic（タムスロシン塩酸塩）が投与された。

The patient's past medications include:

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

ISONIAZIDUM for TUBERCULOSIS PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

RIFAMPICINUM for TUBERCULOSIS PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLONE for ULCERATIVE COLITIS and 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])

CIPROFLOXACINE for EXACERBATION OF CHRONIC PROSTATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Tuberculosis of intrathoracic lymph nodes (10044846) (Tuberculosis of intrathoracic lymph nodes (10044846)) [v.22.0] [10044846]

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) Lymphadenopathy thoracic (10025208) (Lymphadenopathy (10025197)) [v.22.0] [10025208]

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

3) 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 40MG/0.8ML (Blinded)

Event of TUBERCULOSIS OF THE INTRATHORACIC LYMPH NODES

- Investigator: At the start of event there was a suspicion tuberculosis.

- AbbVie: Not applicable

Event of LYMPHADENOPATHY OF UNKNOWN ORIGIN OF THORACIC CAVITY

- Investigator: Not applicable

- AbbVie: Event is more likely related to tuberculosis of intrathoracic lymphnodes.

Event of UC EXACERBATION

- Investigator: Not applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD PRESSURE: 110/70 mmHg

[redacted] 20[redacted] BODY TEMPETURE: 38.5 Degrees C

[redacted] 20[redacted] BODY TEMPERATURE: 38.5 Degrees C

[redacted] 20[redacted] BRONCHOSCOPY: Significant dystrophic changes in the mucosa of bronches & Trachea

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

[redacted] 20[redacted] CT SCAN: signs of multiple spleen formations (Sarcoidosis) miliary focal changes of both lungs, mediastinal and bronchopulmonary bilateral lymphadenopathy.

[redacted] 20[redacted] CT SCAN: expressed intrathoracic lymphadenopathy (at that time malignant lymphoma was questioned), focal dissemination in the lungs and spleen. Bullous emphysema of the lung. Hepatosplenomegaly. The formation of the left adrenal gland is probably an adenoma

[redacted] 20[redacted] HEMOGLOBIN: 138.3 G/DL (normal 13.2 to 17)

[redacted] 20[redacted] HIV TEST: Not reported

[redacted] 20[redacted] MEDIASTINOSCOPY, BIOPSY OF PARATRACHEAL LYMPH NODES: in paratracheal lymph nodes the phenotype of the process corresponds to foci of caseous necrosis with the presence of acid-fast mycobacteria, without a specific granulating shaft, in the phase of compaction and scarring

[redacted] 20[redacted] MRI OF THE HEAD: discirculatory encephalopathy, mild external hydrocephalus

[redacted] 20[redacted] PULSE: 60

[redacted] 20[redacted] QUANTIFERON TB: Positive

[redacted] 20[redacted] SPIRAL COMPUTERTOMOGRAPHIE: Hypersensitive pneumonitis

[redacted] 20[redacted] SPUTUM CULTURE AND ANTIBIOTIC SENSITIVITY: Positive Staphyloccocus hemolyticus

[redacted] 20[redacted] ULTRASOUND OF ABDOMINAL CAVITY & KIDNEYS: Hepatomegalia, splenome galia, chronic cholecystitis,Syndrome of hypoechoic spleen formations of unkown origin

[redacted] 20[redacted] US OF HEART: without echopathology ejection fraction 67%

[redacted] 20[redacted] X-RAY: Big area of the infiltration in the sac on right with the few decay sectors (max 2.5 cm). Medium intensity ficis on the rest of both sides. Mediastinum is extended in the thoracic cavity due to intrathoracic lymph nodes.

[redacted] 20[redacted] X-RAY: Positive dinamics (no other description available)

[redacted] 20[redacted] X-RAY: Positive dinamics (no other description available)

[redacted] 20[redacted] X-RAY: Positive dinamics (no other description available)

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
肺炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	MALE	White

Medical History	Onset Year
ANEMIA: ANEMIA OF CHONIC DISEASE	20[redacted]
OTHER: CHRONIC GASTRODUODENITIS	20[redacted]
OTHER: VASOMOTORICAL RHINITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.5 PACKS	12	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 4040 MG MG EVERY		EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 190	134

WEEK

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	500 mg (milligram(s))	TID	Y-M: 20[redacted]
PREDNISOLONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -172
MACROGOL	200 g (gram(s))	Other: TO DISSOLVE IN 2L OF WATER AND TO TAKE 100 ML EVERY 30 MIN FROM 3 P.M TILL 7 P.M.	Y-M: 20[redacted] / -16

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	500 mg (milligram(s))	TID	Y-M: 20[redacted]	ONGOING
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 45
PREDNISOLONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 60
PARACETAMOL	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 81
REOSORBILACT	200 mL (millilitre(s))	QD	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 82
CEFTRIAXONE	1 g (gram(s))	Other: 2 GR AT 10 A.M.+ 1 G AT 10 P.M.	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 86
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 86
AMBROXOL	15 mL (millilitre(s))	TID	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 89
FLUCONAZOLE	100 mL (millilitre(s))	QD	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 89

Event #1: Serious Adverse Event

Event Description	RIGHT SIDED COMMUNITY-ACQUIRED PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 73
Age at AE Onset	2[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 49): URINE BLOOD: 100 [NOT REPORTED - NOT REPORTED] CELLS ERITHROCYTES; [redacted]20[redacted] (RX DAY 78): HEMOGLOBIN: 136 [130 - 160] G/L; WHITE BLOOD COUNT: 5.9 [4 - 9] X10^9/L; [redacted]20[redacted] (RX DAY 79): ALANINE AMINO TRANSFERASE (SGPT/ALT): 0.2 [0.1 - 0.68] MCMOL/HOUR*ML; ALBUMIN: 43 [35 - 50] G/L; C-REACTIV PROTEINE: 24 [0 - 5] MG/DL; CALCIUM: 2.05 [2.1 - 2.5] MMOL/L; CHLORINE: 101 [95 - 110] MMOL/L; CREATININE: 97 [62 - 115] MCMOL/L; POTASSIUM: 6.7 [3.6 - 5.3] MMOL/L; SODIUM: 136 [137 - 150] MMOL/L; TOTAL BILIRUBIN: 9 [5 - 21] MCMOL/L; URINE GLUCOSE: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; URINE PROTEIN (DIPSTICK TEST): 0.045 [NOT REPORTED - NOT REPORTED] G/L; URINE SPECIFIC GRAVITY: 1.025 [1.003 - 1.035] N/A; [redacted]20[redacted] (RX DAY 84): HEMOGLOBIN: 147 [130 - 160] G/L; WHITE BLOOD COUNT: 6.4 [4 - 9] X10^9/L; [redacted]20[redacted] (RX DAY 85): CREATININE: 100 [62 - 115] MCMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 78): CT SCAN: RT SIDED PNEUMONIA; [redacted]20[redacted] (RX DAY 79): ECG: SINUS RHYTHM; [redacted]20[redacted] (RX DAY 81): ULTRASOUND: THERE ARE NO PATHOLOGICAL CHANGES OF THE OBSERVED ORGANS; [redacted]20[redacted] (RX DAY 88): X-RAY OF THE THORACIC CAVITY: HEART, LUNGS- NORMAL

AE Stopped Rx Day	89
Duration of AE	17 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	AFTER HE CAUGHT IN THE RAIN,HE HAD SORE THROAT, NAZAL CONGESTION, T-39 C,DRY COUGH.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（ウクライナ）であり，重篤な有害事象の市中感染性右側肺炎が認められた。関連する病歴は，慢性疾患性貧血，慢性胃十二指腸炎，及び潰瘍性大腸炎であった。被験者は喫煙者（1 日当たり 0.5 箱，喫煙期間 12 年）であり，非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，市中感染性右側肺炎が認められた。

本被験者は雨に降られて風邪を引いた。20[redacted] 年 [redacted] 月 [redacted] 日より，咽喉痛，鼻閉，及び発熱（39.0°C）が認められた。被験者はアセトアミノフェンを服用した。20[redacted] 年 [redacted] 月 [redacted] 日，夜に発

熱（39.6°C），軽度の乾性咳嗽，及び戦慄が認められ，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，市中感染性右側肺炎は回復した。
治療薬としてレボフロキサシン，アセトアミノフェン，Rheosorbilact，及びセフトリアキソンが投与された。

Causality for HUMIRA (Blinded)

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1) Community acquired pneumonia (10010120) (Pneumonia (10035664)) [v.22.0] [10010120]

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 RIGHT SIDED COMMUNITY-ACQUIRED PNEUMONIA

- Investigator: AFTER HE CAUGHT IN THE RAIN, HE HAD SORE THROAT,NASAL CONGESTION, T-39 C,DRY COUGH.

- AbbVie: NOT APPLICABLE

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] 20[redacted] C REACTIVE PROTEIN: 24 mg/dL (normal 0 to 5)

[redacted] 20[redacted] CALCIUM: 2.05 MMOL/L (normal 2.10 to 2.50)

[redacted] 20[redacted] CHEST XRAY: heart , lungs - normal

[redacted] 20[redacted] CREATININE: 97.1 MCMOL/L (normal 62 to 115)

[redacted] 20[redacted] CT SCAN: Rt sided Pneumonia

[redacted] 20[redacted] ECG: sinus rhythm

[redacted] 20[redacted] HEMOGLOBIN: 136 G/L (normal 130 to 160)

[redacted] 20[redacted] HEMOGLOBIN: 147 G/L (normal 130 to 160)

[redacted] 20[redacted] POTASSIUM: 6.7 nmol/l (normal 3.60 to 5.30)

[redacted] 20[redacted] SODIUM: 136.4 mmol/l (normal 137 to 150)

[redacted] 20[redacted] ULTRASOUND: no pathological changes of the observed organs

[redacted] 20[redacted] WBC: 5.85 X10**9/L (normal 4.0 to 9.0)

[redacted] 20[redacted] WBC: 6.43 X10**9/L (normal 4.0 to 9.0)

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
血栓性静脈炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	MALE	Asian

Medical History	Onset Year
OTHER: ATOPIC DERMATITIS	19[redacted]
OTHER: GASTRITIS ATROPHIC	20[redacted]
OTHER: HYPERAMYLASEMIA	20[redacted]
ASTHMA	NOT REPORTED
OTHER: HETERO TYPE PROTEIN C DEFICIENCY	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 45	45
ADALIMUMAB 4040 MG		EW	[redacted]20[redacted] /	[redacted]20[redacted] /	304

MG EVERY WEEK		57	360

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BIFIDOBACTERIUM LACTIS	1 g (gram(s))	TID	Y-M: 20[redacted] / -197
MESALAZINE	2000 mg (milligram(s))	BID	Y-M: 20[redacted] / -159
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -134
AZATHIOPRINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -107
IRON	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -107
HYOSCINE	10 mg (milligram(s))	PRN	Y-M: 20[redacted] / -33
LOXOPROFEN	60 mg (milligram(s))	PRN	Y-M: 20[redacted] / -33
MAGNESIUM CITRATE	50 g (gram(s))	QD	Y-M: 20[redacted] / -21
SODIUM PICOSULFATE	10 mL (millilitre(s))	QD	Y-M: 20[redacted] / -21
FLUMAZENIL	0.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -20
LIDOCAINE	30 mL (millilitre(s))	QD	Y-M: 20[redacted] / -20
MIDAZOLAM	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -20
MOVIPREP	244.212 g (gram(s))	QD	Y-M: 20[redacted] / -20
PENTAZOCINE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -20
TIMEPIDIUM	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -20

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	2000 mg (milligram(s))	BID	Y-M: 20[redacted] / -159	ONGOING
AZATHIOPRINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -107	ONGOING
LOXOPROFEN	60 mg (milligram(s))	PRN	Y-M: 20[redacted] / -33	ONGOING
BIOFERMIN	1 g (gram(s))	TID	Y-M: 20[redacted] / 1	ONGOING
CELECOXIB	100 mg (milligram(s))	PRN	Y-M: 20[redacted] / 87	ONGOING
DIAZEPAM	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 153	ONGOING
RABEPRAZOLE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 153	ONGOING
HEPARIN	18000 IU (international unit(s))	Other: 24HOURS	Y-M: 20[redacted] / 183	Y-M: 20[redacted] / 183

HEPARIN	20000 IU (international unit(s))	Other: 24HOURS	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 184
WARFARIN	3 mg (milligram(s))	QD	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 188
HEPARIN	22000 IU (international unit(s))	Other: 24HOURS	Y-M: 20[redacted] / 185	Y-M: 20[redacted] / 185
HEPARIN	20000 IU (international unit(s))	Other: 24HOURS	Y-M: 20[redacted] / 186	Y-M: 20[redacted] / 188
WARFARIN	4 mg (milligram(s))	QD	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 194
WARFARIN	3.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 195	Y-M: 20[redacted] / 198
WARFARIN	3.75 mg (milligram(s))	QD	Y-M: 20[redacted] / 199	Y-M: 20[redacted] / 240
WARFARIN	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 241	ONGOING
HYOSCINE	10 mg (milligram(s))	PRN	Y-M: 20[redacted] / 247	ONGOING
RAMOSETRON	5 mcg (microgram(s))	PRN	Y-M: 20[redacted] / 331	ONGOING
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 349

Event #1: Serious Adverse Event

Event Description	LEFT SUBCLAVICULAR VENOUS THROMBOPHLEBITIS
Preferred term	血栓性静脈炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 183
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 1): MPO-ANCA-ST: 23.6 [NOT REPORTED - 3.5] U/ML; PR3-ANCA-ST: 42.7 [NOT REPORTED - 3.5] U/ML; [redacted]20[redacted] (RX DAY 183): MPO-ANCA-ST: 36.4 [NOT REPORTED - 3.5] U/ML; PR3-ANCA-ST: 53.3 [NOT REPORTED - 3.5] U/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility

Investigator Alternative Etiology	UC HETERO TYPE PROTEIN C DEFICIENCY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（日本）であり，重篤な有害事象の左鎖骨下静脈の血栓性静脈炎が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］）及びヘテロ接合体性プロテイン C 欠乏症であった。
20[redacted] 年 [redacted] 月より，左胸及び左上肢の疼痛が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，左鎖骨下静脈の血栓性静脈炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，左胸及び左上肢の疼痛，並びに左下肢の浮腫の兆候及び症状が認められ，被験者は入院した。被験者は血栓性静脈炎と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，抗凝固治療が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，ワルファリン経口剤により血栓性静脈炎が管理可能となったため，被験者は退院した。
治療薬としてワルファリン及びヘパリンが投与された。

The patient's past medications include:

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

Causality for HUMIRA (Open Label)

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1) Venous thrombophlebitis (10047247) (Thrombophlebitis (10043570)) [v.18.1] [10047247]

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

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of LEFT SUBCLAVICULAR VENOUS THROMBOPHLEBITIS

- Investigator: Ulcerative colitis

- AbbVie: The patient has a positive medical history of protein C Difficiency that is a rare genetic disease assoaciated with an increased incidence of venous thromboembolism

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Screening - Endoscopy: Rectum 1 = Mild disease (erythema, decreased vascular pattern, mild friability). Sigmoid 3 = Severe disease (spontaneous bleeding, ulceration). Descending colon 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions). Transverse colon 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions). Ascending colon/cecum 1 = Mild disease (erythema, decreased vascular pattern, mild friability). Presence of friability? Yes. Subscore 3.

[redacted] 20[redacted] Colonoscopy:

Week 8 (1) - Endoscopy: Rectum 1 = Mild disease (erythema, decreased vascular pattern, mild friability). Sigmoid 1 = Mild disease (erythema, decreased vascular pattern, mild friability). Descending colon 1 = Mild disease (erythema, decreased vascular pattern, mild friability). Transverse colon 0 = Normal or inactive disease. Ascending colon/cecum 0 = Normal or inactive disease. Presence of friability?

Yes. Subscore 1.

[redacted] 20[redacted] MPO-ANCA-ST: 23.6 U/ML (normal < 3.5)

[redacted] 20[redacted] MPO-ANCA-ST: 36.4 U/ML (normal < 3.5)

[redacted] 20[redacted] PR3-ANCA-ST: 42.7 U/ML (normal < 3.5)

[redacted] 20[redacted] PR3-ANCA-ST: 53.3 U/ML (normal < 3.5)

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	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	4[redacted]	MALE	Asian

Medical History	Onset Year
OTHER: RHINITIS	19[redacted]
OTHER: STEROID-INDUCED FEMUR HEAD NECROSIS,LT	20[redacted]
SURGERY: TOTAL HIP ARTHROPLASTY,LT	20[redacted]
OTHER: ANXIETY NEUROSIS	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: OSTEOARTHRITIS OF THE KNEE, RT	20[redacted]
SURGERY: OSTEOARTHRITIS OF THE KNEE,RT	20[redacted]
OTHER: AZATHIOPRINE-INDUCED LIVER INJURY	20[redacted]
OTHER: HIP OSTEOARTHRITIS,RT	20[redacted]
SURGERY: HIP OSTEOARTHRITIS,RT	20[redacted]
OTHER: MULTIFOCAL POSTERIOR PIGMENT EPITHELIOPATHY	20[redacted]
OTHER: REFLUX ESOPHAGITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 218	162

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
TRIMEBUTINE	100 mg (milligram(s))	TID	Y-M: 19[redacted]
AZELASTINE	1 mg (milligram(s))	BID	Y-M: 19[redacted]
TOFISOPAM	50 mg (milligram(s))	TID	Y-M: 19[redacted]
RABEPRAZOLE	10 mg (milligram(s))	QD	Y-M: 20[redacted]
ALENDRONIC ACID	35 mg (milligram(s))	Other: ONCE PER WEEK	Y-M: 20[redacted]-[redacted]
BROTIZOLAM	0.25 mg (milligram(s))	QD	Y-M: 20[redacted]
CLOTIAZEPAM	5 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted]
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -274
CLOSTRIDIUM BUTYRICUM	1 TABLET	TID	Y-M: 20[redacted]-[redacted] / -274
PA	1 PACK	PRN	Y-M: 20[redacted]-[redacted] / -242
POVIDONE-IODINE	PRN APPLICATION	PRN	Y-M: 20[redacted]-[redacted] / -242
PREDNISOLONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -130
MERCAPTOPURINE	25 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -102
MERCAPTOPURINE	30 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -74
PREDNISOLONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -74
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -46
GLYCEROL	120 mL (millilitre(s))	PRN	Y-M: 20[redacted]-[redacted] / -29
HYOSCINE	20 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / -29
LIDOCAINE	30 mL (millilitre(s))	PRN	Y-M: 20[redacted]-[redacted] / -29
MERCAPTOPURINE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -29
PREDNISOLONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -29
SORBIT HARTMAN	300 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / -29
BACTRIM	1 TABLET	QD	Y-M: 20[redacted]-[redacted] / -18
PREDNISOLONE	20 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -18

SODIUM PICOSULFATE	10 mL (millilitre(s))	PRN	Y-M: 20[redacted] / -13
BARIUM	5 mL (millilitre(s))	PRN	Y-M: 20[redacted] / -12
COLYTE	137.155 g (gram(s))	PRN	Y-M: 20[redacted] / -12
DIAZEPAM	7.5 mg (milligram(s))	PRN	Y-M: 20[redacted] / -12
HYOSCINE	20 mg (milligram(s))	PRN	Y-M: 20[redacted] / -12
INDIGO CARMINE	20 mL (millilitre(s))	PRN	Y-M: 20[redacted] / -12
LIDOCAINE	30 mL (millilitre(s))	PRN	Y-M: 20[redacted] / -12
PREDNISOLONE	15-5 mg (milligram(s))	BID	Y-M: 20[redacted] / -7
FLUORESCEIN	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / -4
INDOCYANINE GREEN	25 mg (milligram(s))	PRN	Y-M: 20[redacted] / -4

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
TRIMEBUTINE	100 mg (milligram(s))	TID	Y-M: 19[redacted]	ONGOING
AZELASTINE	1 mg (milligram(s))	BID	Y-M: 19[redacted]	ONGOING
TOFISOPAM	50 mg (milligram(s))	TID	Y-M: 19[redacted]	ONGOING
RABEPRAZOLE	10 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
ALENDRONIC ACID	35 mg (milligram(s))	Other: ONCE PER WEEK	Y-M: 20[redacted]	ONGOING
CLOTIAZEPAM	5 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted]	ONGOING
CLOSTRIDIUM BUTYRICUM	1 TABLET	TID	Y-M: 20[redacted] / -274	ONGOING
POVIDONE-IODINE	PRN APPLICATION	PRN	Y-M: 20[redacted] / -242	ONGOING
MERCAPTOPURINE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -29	ONGOING
POLYCARBOPHIL	1000 mg (milligram(s))	TID	Y-M: 20[redacted] / 21	ONGOING
MEPENZOLATE	15 mg (milligram(s))	TID	Y-M: 20[redacted] / 23	ONGOING
NADIFLOXACIN	PRN APPLICATION	PRN	Y-M: 20[redacted] / 32	ONGOING
PA	1 PACK	PRN	Y-M: 20[redacted] / 36	ONGOING
LOXOPROFEN	60 mg (milligram(s))	PRN	Y-M: 20[redacted] / 85	ONGOING
ESZOPICLONE	3 mg (milligram(s))	QD	Y-M: 20[redacted] / 134	ONGOING

PREDNISOLONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 156	ONGOING
BROTIZOLAM	0.25 mg (milligram(s))	QD	Y-M: 20[redacted] / 169	ONGOING
IRON	105 mg (milligram(s))	QD	Y-M: 20[redacted] / 169	Y-M: 20[redacted] / 203
LOPERAMIDE	1 mg (milligram(s))	QD	Y-M: 20[redacted] / 185	Y-M: 20[redacted] / 204
POSTERISAN F	2 g (gram(s))	PRN	Y-M: 20[redacted] / 185	Y-M: 20[redacted] / 204
HYOSCINE	20 mg (milligram(s))	PRN	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 204
INDIGO CARMINE	20 mL (millilitre(s))	PRN	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 204
ACMAIN	500 mL (millilitre(s))	PRN	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 226
BARIUM	5 mL (millilitre(s))	PRN	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 226
DIAZEPAM	10 mg (milligram(s))	PRN	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 226
HYOSCINE	20 mg (milligram(s))	PRN	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 226
INDIGO CARMINE	20 mL (millilitre(s))	PRN	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 226
INDIGO	1 g (gram(s))	BID	Y-M: 20[redacted] / 227	Y-M: 20[redacted] / 238
INDIGO	1.5-1 g (gram(s))	BID	Y-M: 20[redacted] / 239	Y-M: 20[redacted] / 239
INDIGO	1.5 g (gram(s))	BID	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 245
INDIGO	1.5-1 g (gram(s))	BID	Y-M: 20[redacted] / 246	Y-M: 20[redacted] / 246
INDIGO	1 g (gram(s))	BID	Y-M: 20[redacted] / 247	Y-M: 20[redacted] / 256
INDIGO	1.5 g (gram(s))	BID	Y-M: 20[redacted] / 257	ONGOING
BETAMETHASONE	1 mg (milligram(s))	QD	Y-M: 20[redacted] / 280	ONGOING

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

Event Description	UC AGGRAVATION
Preferred term	潰瘍性大腸炎

AE Onset Date / Rx Day	[redacted]20[redacted] / 225 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 225): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.19 [NOT REPORTED - 0.14] MG/DL	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	LOSS OF RESPONSE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[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。関連する病歴は，左側潰瘍性大腸炎，不安神経症，及び不眠症であった。

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，被験者は入院した。血便，腹痛，及び排便頻度の増加を含む兆候及び症状が認められた。入院後，20[redacted] 年 [redacted] 月 [redacted] 日よりインジゴ・ナチュラリス（1 日当たり 2 g）の経口投与による治療が開始され，20[redacted] 年 [redacted] 月 [redacted] 日に用量が 1 日当たり 3 g に増量された。血便及び腹痛は徐々に回復した。また，排便頻度も減少した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Rinderon（ベタメタゾン吉草酸エステル／ゲンタマイシン硫酸塩）及びインジゴ・ナチュラリスが投与された。

The patient's past medications include:

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

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

Causality for HUMIRA (Blinded)

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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

Alternative Etiology for HUMIRA (Blinded)

Event of UC EXACERBATION

- Investigator: LOSS OF RESPONSE.

- AbbVie: THE EVENT IS RELATED TO THE COURSE OF UNDERLYING DISEASE.

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			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	2[redacted]	MALE	Asian

Medical History	Onset Year
Not reported.	

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.5 PACKS	3	
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 36	36
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CLOSTRIDIUM BUTYRICUM	20 mg (milligram(s))	TID	Y-M: 20[redacted] / -170
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted] / -156
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -132
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -89
PREDNISOLONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -80
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -68
MERCAPTOPURINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -55
FOSFOMYCIN	2 g (gram(s))	QD	Y-M: 20[redacted] / -35
METHYLPREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -35
PREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -35
DIAZEPAM	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -15
HYOSCINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -15
INFLUENZA VACCINE	0.5 mL (millilitre(s))	QD	Y-M: 20[redacted] / -15
MAGNESIUM CITRATE	100 g (gram(s))	QD	Y-M: 20[redacted] / -15
PETHIDINE	35 mg (milligram(s))	QD	Y-M: 20[redacted] / -15

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CLOSTRIDIUM BUTYRICUM	20 mg (milligram(s))	TID	Y-M: 20[redacted] / -170	ONGOING
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted] / -156	ONGOING
MERCAPTOPURINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -55	ONGOING
PREDNISOLONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 113
PREDNISOLONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 155
FOSFOMYCIN	2 g (gram(s))	QD	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 130
LOXOPROFEN	60 mg (milligram(s))	QD	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 130
METOCLOPRAMIDE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 130
OSMOSAL	1500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 130

METOCLOPRAMIDE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 132
SOLITA-T1	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 133
FOSFOMYCIN	2 g (gram(s))	BID	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 137

Event #1: Serious Adverse Event

Event Description	INFECTIONS GASTROENTERO COLITIS
Preferred term	胃腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 130
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 130): C.DIFFICILE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 2.9 [0 - 3] MG/L; WHITE BLOOD COUNT: 12.8 [3.6 - 9] X10^9/L; [redacted]20[redacted] (RX DAY 131): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 35.7 [0 - 3] MG/L; WHITE BLOOD COUNT: 9 [3.6 - 9] X10^9/L; [redacted]20[redacted] (RX DAY 133): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 9.8 [0 - 1.3] MG/L; WHITE BLOOD COUNT: 6.6 [3.6 - 9] X10^9/L; [redacted]20[redacted] (RX DAY 138): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 1 [0 - 3] MG/L; WHITE BLOOD COUNT: 8.3 [3.6 - 9] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 130): Stool BACTERIA TEST: P-STAPHYLOCOCCUS AUREUS

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	138
Duration of AE	9 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ACUTE INFECTIONS DISEASE BY STAPHYLOCOCCUS AUREUS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（日本）であり，重篤な有害事象の感染性胃小腸大腸炎が認められた。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，感染性胃小腸大腸炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，発熱及び嘔吐が認められた。被験者は，感染性胃小腸大腸炎と診断された。被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，感染性胃小腸大腸炎は回復した。同日に被験者は退院した。

治療薬として Loxonin（ロキソプロフェンナトリウム水和物），Fosmicin S（ホスホマイシンカルシウム水和物），Soldem 1，Primperan（塩酸メトクロプラミド），及びプレドニゾロンが投与された。

The patient's past medications include:

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

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

SOL-MELCORT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BUSCOPAN for ENDOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

HORIZON for ENDOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

MACROGOL for ENDOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted])

OPYSTAN for ENDOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

GASCON for ENDOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted])

MOVEPREP for ENDOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Gastroenterocolitis (10059169) (Gastroenteritis (10017888)) [v.18.0] [10059169]

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

Alternative Etiology for HUMIRA (Open Label)

Event of INFECTIONS GASTROENTERO COLITIS

- Investigator: Acute infectious disease by Staphyloccoccus aureus.

- AbbVie: Patient with infectious gastroenterocolitis due to Clostridium difficile.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Stool culture: C Difficile negative

[redacted] 20[redacted] Stool culture: positive for Staphyloccoccus aureus

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 EVERY WEEK	3[redacted]	MALE	Asian

Medical History	Onset Year
CHOLELITHIASIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	13	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 41	41
ADALIMUMAB 4040 MG MG EVERY WEEK		EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 105	49

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BIO-THREE	2 TABLET	TID	Y-M: 20[redacted] / -339
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted] / -335
PREDNISOLONE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / -309
TACROLIMUS	6 mg (milligram(s))	BID	Y-M: 20[redacted] / -151
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -129
ESOMEPRAZOLE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -105
SENNOSIDE A+B	24 mg (milligram(s))	QD	Y-M: 20[redacted] / -18
HYOSCINE	20 mg (milligram(s))	PRN	Y-M: 20[redacted] / -17
LIDOCAINE	5 mL (millilitre(s))	PRN	Y-M: 20[redacted] / -17
METOCLOPRAMIDE	1 TABLET	PRN	Y-M: 20[redacted] / -17
MOVIPREP	1 PAC	PRN	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
BIO-THREE	2 TABLET	TID	Y-M: 20[redacted] / -339	ONGOING
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted] / -335	ONGOING
ESOMEPRAZOLE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -105	ONGOING
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 91
IRON	105 mg (milligram(s))	QD	Y-M: 20[redacted] / 99	ONGOING
CEFOZOPRAN	1 g (gram(s))	PRN	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
PREDNISOLONE	30 mg (milligram(s))	PRN	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
PREDNISOLONE	30 mg (milligram(s))	BID	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 135
INFLIXIMAB	300 mg (milligram(s))	PRN	Y-M: 20[redacted] / 133	ONGOING
PREDNISOLONE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / 136	Y-M: 20[redacted] / 146

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

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 112 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	

NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	169 (64 DAYS AFTER LAST TREATMENT)
Duration of AE	58 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UC
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[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悪化が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 13 年）であり，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，被験者の容体が悪化（下痢，腹痛，及び発熱）した。20[redacted] 年 [redacted] 月 [redacted] 日，Predonine（プレドニゾロンコハク酸エステルナトリウム）30 mg 及び Firstcin（セフォゾプラン塩酸塩）静注用 1 g の静脈内投与による治療が実施された。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に入院し，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。

また，20[redacted] 年 [redacted] 月 [redacted] 日～20[redacted] 年 [redacted] 月 [redacted] 日の間に非重篤な気管支炎が認められていた。

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），Firstcin（セフォゾプラン塩酸塩），及び Remicade（インフリキシマブ）が投与された。

The patient's past medications include:

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

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

PENTASA 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: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: UC

- AbbVie: THE EVENT IS EXACERBATION OF UNDERLYING DISEASE.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Colonoscopy: Rectum: 3 = severe disease (spontaneous bleeding, ulceration); Sigmoid/Descending colon: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions); Transverse colon: 1 = mild disease (erythema, decreased vascular pattern, mild friability); Ascending colon/cecum: 0 = normal or inactive disease. Friability present. Subscore = 3.

[redacted] 20[redacted] Electrocardiogram: Normal

[redacted] 20[redacted] Flexible sigmoidoscopy:

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

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
意識変容状態	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	4[redacted]	MALE	Asian

Medical History	Onset Year
HYPERTENSION	NOT REPORTED
OTHER: GASTRITIS	NOT REPORTED
OTHER: LOW BACK PAIN	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 4040 MG MG EVERY OTHER WEEK		EOW	[redacted]20[redacted] / 59	[redacted]20[redacted] / 162	104

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
LOXOPROFEN	100 APPLICATION	QD	Y-M: 20[redacted]
OLMESARTAN	10 mg (milligram(s))	QD	Y-M: 20[redacted]
VONOPRAZAN	20 mg (milligram(s))	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg (milligram(s)/kilogram)	Other: ONCE PER 2 WEEKS	Y-M: 20[redacted]-[redacted] / -160
PREDNISOLONE	35 mg (milligram(s))	Other: DAILY	Y-M: 20[redacted]-[redacted] / -59
CELECOXIB	100 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -49
CLOSTRIDIUM BUTYRICUM	40 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / -49
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -42
IRON	50 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -42
TRAMADOL	50 mg (milligram(s))	QID	Y-M: 20[redacted]-[redacted] / -42
DIMETICONE	20 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -19
FLUMAZENIL	0.5 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -19
GLUCOSE	100 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -19
HYOSCINE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -19
MIDAZOLAM	10 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -19
MOVIPREP	1 APPLICATION	Other: ONCE	Y-M: 20[redacted]-[redacted] / -19
NALOXONE	0.2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -19
PETHIDINE	35 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -19

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted]	ONGOING
VONOPRAZAN	20 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
CELECOXIB	100 mg (milligram(s))	BID	Y-M: 20[redacted] / -49	ONGOING
CLOSTRIDIUM BUTYRICUM	40 mg (milligram(s))	TID	Y-M: 20[redacted] / -49	ONGOING
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -42	ONGOING
IRON	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -42	ONGOING
OLMESARTAN	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 9	ONGOING
TRAMADOL	300 mg (milligram(s))	Other: DAILY	Y-M: 20[redacted] / 22	ONGOING
HYALURONIC ACID	1 gtt (drop(s))	QID	Y-M: 20[redacted] / 39	ONGOING
LATANOPROST	1 gtt (drop(s))	QD	Y-M: 20[redacted] / 39	ONGOING
IBANDRONIC ACID	100 mg (milligram(s))	Other: ONCE A MONTH	Y-M: 20[redacted] / 67	ONGOING
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	1 APPLICATION	QD	Y-M: 20[redacted] / 67	ONGOING
PREDNISOLONE	10 mg (milligram(s))	Other: DAILY	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 85
PREDNISOLONE	5 mg (milligram(s))	Other: DAILY	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 134
ALPRAZOLAM	0.4 mg (milligram(s))	BID	Y-M: 20[redacted] / 110	ONGOING
BROTIZOLAM	0.25 mg (milligram(s))	QD	Y-M: 20[redacted] / 110	ONGOING

Event #1: Serious Adverse Event

Event Description	DISTURBANCE OF CONSCIOUSNESS
Preferred term	意識変容状態
AE Onset Date / Rx Day	[redacted]20[redacted] / 110
Age at AE Onset	4[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 110): BUN: 8 [2.9 - 7.9] MMOL/L; C-REACTIVE PROTEIN: 1.3 [NOT REPORTED - 0.3] MG/DL; CREATINE PHOSPHOKINASE: 301 [62 - 287] U/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	113
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（日本）であり，重篤な有害事象の意識障害が認められた。関連する病歴は，潰瘍性大腸炎及び腰痛であった。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は緑内障（非重篤）と診断された（継続中）。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腰椎圧迫骨折（非重篤）と診断された（継続中）。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は骨粗鬆症（非重篤）と診断された（継続中）。
20[redacted] 年 [redacted] 月 [redacted] 日，意識障害が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，意識障害は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，不眠症（非重篤），脱水，及び C 反応性たん白値上昇の症状が認められ，意識障害と判断されて被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Solanax（アルプラゾラム）及びブロチゾラムが投与された。

Causality for HUMIRA (Blinded)

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1) Consciousness disturbed (10010770) (Altered state of consciousness (10001854)) [v.20.0] [10010770]

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 DISTURBANCE OF CONSCIOUSNESS

- Investigator: N/A

- AbbVie: The patient's concomitant medication Includes Tramal, an Opioid Analgesic Which Affects Serotonin Reuptake And Could Potentially Have CNS Implications.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BUN: 22.5 mg/dL (normal 8 to 22)

[redacted] 20[redacted] C REACTIVE PROTEIN: 1.3 mg/dL (normal <0.3)

[redacted] 20[redacted] CREATINE PHOSPHOKINASE: 301 IU/L (normal 62 to 287)

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
ADALIMUMAB 40 MG EVERY WEEK	4[redacted]	FEMALE	Asian

Medical History	Onset Year
LIVER DISEASE (EXCLUDING HEPATITIS): AZA INDUCED HEPATIC ENZYME INCREASED	NOT REPORTED
OTHER: LUMBAR SPONDYLOLISTHESIS	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB 4040 MG MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 210	155

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted] / -305
CLOSTRIDIUM BUTYRICUM	40 mg (milligram(s))	TID	Y-M: 20[redacted] / -217
PREDNISOLONE	17.5 mg (milligram(s))	BID	Y-M: 20[redacted] / -217
RABEPRAZOLE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -217
ALFACALCIDOL	1 mcg (microgram(s))	QD	Y-M: 20[redacted] / -183
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -146
PREDNISOLONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -49
SENNOSIDE A+B	36 mg (milligram(s))	QD	Y-M: 20[redacted] / -16
DIMETICONE	10 mL (millilitre(s))	QD	Y-M: 20[redacted] / -15
FLUMAZENIL	0.2 mg (milligram(s))	PRN	Y-M: 20[redacted] / -15
GLYCEROL	OPTIMUM APPLICATION	PRN	Y-M: 20[redacted] / -15
HYOSCINE	20 mg (milligram(s))	PRN	Y-M: 20[redacted] / -15
METOCLOPRAMIDE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -15
MIDAZOLAM	6 mg (milligram(s))	PRN	Y-M: 20[redacted] / -15
MOVIPREP	1000 mL (millilitre(s))	PRN	Y-M: 20[redacted] / -15

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted] / -305	ONGOING
CLOSTRIDIUM BUTYRICUM	40 mg (milligram(s))	TID	Y-M: 20[redacted] / -217	ONGOING
RABEPRAZOLE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -217	ONGOING
ALFACALCIDOL	1 mcg (microgram(s))	QD	Y-M: 20[redacted] / 1	ONGOING
MECOBALAMIN	500 mcg (microgram(s))	TID	Y-M: 20[redacted] / 155	ONGOING
NUTRIENTS NOS	200 mL (millilitre(s))	TID	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 251
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 255
LOXOPROFEN	60 mg (milligram(s))	PRN	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 266
TEPRENONE	50 mg (milligram(s))	PRN	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 266
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 255	Y-M: 20[redacted] / 263
TACROLIMUS	3 mg (milligram(s))	BID	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 260
TACROLIMUS	4-4.5 mg (milligram(s))	BID	Y-M: 20[redacted] / 261	Y-M: 20[redacted] / 262
TACROLIMUS	3-3.5 mg (milligram(s))	BID	Y-M: 20[redacted] / 263	Y-M: 20[redacted] / 265

TACROLIMUS	2.5-3 mg (milligram(s))	BID	Y-M: 20[redacted] / 266 Y-M: 20[redacted] / 268
TACROLIMUS	3 mg (milligram(s))	BID	Y-M: 20[redacted] / 269 Y-M: 20[redacted] / 272
TACROLIMUS	3.5 mg (milligram(s))	BID	Y-M: 20[redacted] / 273 Y-M: 20[redacted] / 279

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 248 (38 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	274 (64 DAYS AFTER LAST TREATMENT)
Duration of AE	27 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	INADEQUATE RESPONSE TO UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（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。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，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，排便頻度の増加（1 日当たり 8 回），軽度の腹痛，及び嘔吐のため，被験者は救急治療室を受診した。原因として潰瘍性大腸炎の増悪又は感染症が考えられた。被験者は Soldem 1 の投与後に回復した。20[redacted] 年 [redacted] 月 [redacted] 日より白血球除去療法が開始され，Cravit（レボフロキサシン水和物）錠 500 mg が投与された。排便頻度は増加し（1 日当たり 15～20 回），体温は 38～39°C であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は断食を継続して水分補給をし，Cravit（レボフロキサシン水和物）の静脈内投与が開始された。また，白血球除去療法のため，Prograf（タクロリムス水和物）カプセル 3 mg が投与された。炎症の改善が認められた。Ensure の投与が開始された。Cravit（レボフロキサシン水和物）の静脈内投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は流動食の摂取を開始した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師により，本事象は治験薬投与を中止した後に発現した事象であると判断された。潰瘍性大腸炎の増悪のため，治験薬との因果関係は否定できると判断された。

治療薬として Soldem 1，Cravit（レボフロキサシン水和物），Ensure，RACOL-NF，テプレノン，及び Prograf（タクロリムス水和物）が投与された。

The patient's past medications include:

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

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

Causality for HUMIRA 40MG/0.8ML (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 40MG/0.8ML (Open Label)

Event of EXACERBATION OF UC

- Investigator: Inadequate response to UC.

- AbbVie: The event is exacerbation of underlying UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CRP: 2.03 mg/dL

[redacted] 20[redacted] CRP: 0.49 mg/dL

[redacted] 20[redacted] COLONOSCOPY: Exacerbation to total colitis. Inflammatory response was obviously seen from sigmoid colon to rectum.

Unknown date COMPUTER TOMOGRAPHY: Inflammatory responsewas seen from transverse colon to rectum and no other clear inflammation.

Unknown date CRP: 10.16 mg/dL

[redacted] 20[redacted] WBC: 9600 ML

[redacted] 20[redacted] WBC: 7500 ML

Unknown date WBC: 10400 ML

M11-290 主試験

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： 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	
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）：2014 年 10 月 13 日 治験終了日（最後の被験者の最終来院日）：20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ： 第 III 相
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：93 例 組入れ時：93 例 解析時：93 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しない患者を適格とした。	

治験方法：

M11-290 試験は，副腎皮質ステロイド若しくは免疫抑制剤又はその両方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。

治験実施計画書の改訂 4 版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，規制要件に従い維持療法期の対照群として内部プラセボ群を用いた。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：[redacted]

プラセボ：[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主試験 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主試験 modified ITT-E（mITT-E）集団を対象とした。主試験 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主試験の被験者としたが，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。主試験 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，維持療法期に治験薬の投与を 1 回以上受けたすべての主試験の被験者とした。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。

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主試験の被験者を主試験安全性解析対象集団と定義し，安全性の解析対象とした。有害事象は投与群別に記述統計量を用いて要約した。重篤な有害事象，並びに死亡に至った有害事象及び治験薬投与の中止に至った有害事象などの特に注目すべき有害事象を，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」）別に集計した。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：

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 及び 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 I-HD 群及び I-SD 群の併合群，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 M-HD 群及び M-SD 群の併合群，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。

薬物動態：

別途報告書に記載することとした。

安全性：

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。

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。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。

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)

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.)				
胃食道逆流性疾患	0	1 (2.1)	1 (6.3)	2 (2.2)
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)

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.)				
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)
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)
靱帯捻挫	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.

相互参照：M11-290 主試験 中間 CSR Table 14.3__1.2.1.1.1

表 2. 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 2. 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)

表 2. 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.)					
喉頭炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
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)

表 2. 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 (%)
臨床検査(Cont.)					
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)
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 2. 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 2.　　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.

相互参照：M11-290 主試験 中間 CSR Table 14.3__1.2.1.1.2

表 3. 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 3. 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 3. 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 3. 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 3. 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 3. 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 3. 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 3. 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 3. 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 3. 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 3. 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."

相互参照：M11-290 主試験 中間 CSR Table 14.3__1.3.1.1

表 4. 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 4. 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 4. 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 4. 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 4. 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 4. 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 4. 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 4. 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 4. 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 4. 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 4. 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 4. 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 4. 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."

相互参照：M11-290 主試験 中間 CSR Table 14.3__1.3.1.2

M11-290 日本サブ試験

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： [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： 2014 年 10 月 13 日 日本サブ試験：2014 年 12 月 22 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，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） 中間解析時：100 例*（主試験 93 例，日本サブ試験 7 例） *日本サブ試験の被験者 1 例は盲検下での投与を継続中であったため，中間解析に含めなかった。	
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。

治験実施計画書の改訂 4 版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用いた。

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。

有効性の解析は，統合集団（日本以外の施設で登録された被験者［主試験］と日本の施設で登録された被験者［日本サブ試験］を統合）と日本人集団（日本の施設で登録された被験者［日本サブ試験］のみ）の両方を対象

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 100 例，日本人安全性解析対象集団 7 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：

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 I-HD 群及び I-SD 群の併合群，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 M-HD 群及び M-SD 群の併合群，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 I-HD 群及び I-SD 群の併合群，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 群及び M-SD 群の併合群，並びに 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 M-HD 群及び M-SD 群の併合群，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）。

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。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，アダリムマブの投与を受けた被験者では，治験期間中に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：

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 100 例中 80 例に 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重篤な有害事象は導入療法期中に発現せず，維持療法期中に 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）。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。

導入療法期及び維持療法期のいずれも，特に注目すべき有害事象の発現割合は感染症を除き低かった（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，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（最初の疾患再燃前）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）（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=17) n (%)	Total (N=100) n (%)
Any adverse event	19 (59.4)	27 (52.9)	13 (76.5)	59 (59.0)
血液およびリンパ系障害	3 (9.4)	3 (5.9)	1 (5.9)	7 (7.0)
貧血	3 (9.4)	3 (5.9)	1 (5.9)	7 (7.0)
血小板増加症	0	0	1 (5.9)	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 (29.4)	20 (20.0)
腹痛	0	2 (3.9)	2 (11.8)	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 (5.9)	7 (7.0)
便秘	0	0	1 (5.9)	1 (1.0)
下痢	0	0	1 (5.9)	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 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）（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=17) n (%)	Total (N=100) 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 (5.9)	2 (2.0)
血便排泄	0	2 (3.9)	0	2 (2.0)
悪心	0	3 (5.9)	1 (5.9)	4 (4.0)
膵炎	0	1 (2.0)	0	1 (1.0)
嘔吐	0	1 (2.0)	1 (5.9)	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)	0	12 (12.0)
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	0	1 (1.0)
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 (35.3)	23 (23.0)
気管支炎	0	0	1 (5.9)	1 (1.0)

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）（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=17) n (%)	Total (N=100) 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 (5.9)	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 (5.9)	4 (4.0)
レンサ球菌感染	0	0	1 (5.9)	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 (5.9)	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 (5.9)	1 (1.0)
傷害、中毒および処置合併症	4 (12.5)	2 (3.9)	0	6 (6.0)
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)
靭帯捻挫	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 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）（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=17) n (%)	Total (N=100) n (%)
臨床検査	2 (6.3)	2 (3.9)	2 (11.8)	6 (6.0)
血圧上昇	0	1 (2.0)	0	1 (1.0)
C一反応性蛋白増加	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 (5.9)	1 (1.0)
単球数減少	0	0	1 (5.9)	1 (1.0)
好中球数減少	0	0	1 (5.9)	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 (5.9)	1 (1.0)
筋骨格系および結合組織障害	2 (6.3)	2 (3.9)	1 (5.9)	5 (5.0)
関節痛	1 (3.1)	0	1 (5.9)	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 (23.5)	15 (15.0)
頭痛	5 (15.6)	5 (9.8)	4 (23.5)	14 (14.0)
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 (5.9)	2 (2.0)

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）（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=17) n (%)	Total (N=100) n (%)
腎および尿路障害	0	0	1 (5.9)	1 (1.0)
糖尿	0	0	1 (5.9)	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 (17.6)	7 (7.0)
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 (11.8)	4 (4.0)
鼻漏	0	1 (2.0)	1 (5.9)	2 (2.0)
皮膚および皮下組織障害	1 (3.1)	0	1 (5.9)	2 (2.0)
結節性紅斑	1 (3.1)	0	0	1 (1.0)
発疹	0	0	1 (5.9)	1 (1.0)

One patient ([redacted]) who is ongoing study is excluded from interim analysis.
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.

相互参照：M11-290 日本サブ試験 中間 CSR Table 14.3__1.2.1.1.1_A

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）（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=1) n (%)	Total (N=7) n (%)
Any adverse event	2 (100)	4 (100)	1 (100)	7 (100)
眼障害	0	1 (25.0)	0	1 (14.3)
眼瞼炎	0	1 (25.0)	0	1 (14.3)
一般・全身障害および投与部位の状態	2 (100)	1 (25.0)	0	3 (42.9)
異常感	1 (50.0)	0	0	1 (14.3)
注射部位紅斑	0	1 (25.0)	0	1 (14.3)
注射部位疼痛	1 (50.0)	0	0	1 (14.3)
感染症および寄生虫症	0	3 (75.0)	0	3 (42.9)
外耳炎	0	1 (25.0)	0	1 (14.3)
上気道感染	0	2 (50.0)	0	2 (28.6)
臨床検査	0	0	1 (100)	1 (14.3)
単球数減少	0	0	1 (100)	1 (14.3)
好中球数減少	0	0	1 (100)	1 (14.3)
白血球数減少	0	0	1 (100)	1 (14.3)
神経系障害	1 (50.0)	0	0	1 (14.3)
頭痛	1 (50.0)	0	0	1 (14.3)

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）（日本人安全性解析対象集団，M11-290 試験）（続き）

One patient ([redacted]) who is ongoing study is excluded from interim analysis.
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.

相互参照：M11-290 日本サブ試験 中間 CSR Table 14.3__1.2.1.1.1_J

表 3. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
Any adverse event	21 (63.6)	25 (71.4)	46 (67.6)	10 (83.3)	56 (70.0)
血液およびリンパ系障害	4 (12.1)	1 (2.9)	5 (7.4)	2 (16.7)	7 (8.8)
貧血	3 (9.1)	1 (2.9)	4 (5.9)	1 (8.3)	5 (6.3)
リンパ節症	1 (3.0)	0	1 (1.5)	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 (2.9)	1 (1.5)	0	1 (1.3)
耳痛	0	1 (2.9)	1 (1.5)	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 (27.3)	10 (28.6)	19 (27.9)	3 (25.0)	22 (27.5)
腹痛	1 (3.0)	1 (2.9)	2 (2.9)	1 (8.3)	3 (3.8)
上腹部痛	0	2 (5.7)	2 (2.9)	0	2 (2.5)
アフタ性潰瘍	1 (3.0)	0	1 (1.5)	0	1 (1.3)
潰瘍性大腸炎	6 (18.2)	4 (11.4)	10 (14.7)	2 (16.7)	12 (15.0)
便秘	1 (3.0)	0	1 (1.5)	0	1 (1.3)
下痢	0	1 (2.9)	1 (1.5)	0	1 (1.3)
消化不良	0	1 (2.9)	1 (1.5)	0	1 (1.3)
小腸炎	2 (6.1)	1 (2.9)	3 (4.4)	0	3 (3.8)
胃食道逆流性疾患	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 3. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
一般・全身障害および投与部位の状態	5 (15.2)	3 (8.6)	8 (11.8)	1 (8.3)	9 (11.3)
胸痛	0	1 (2.9)	1 (1.5)	0	1 (1.3)
疲労	2 (6.1)	0	2 (2.9)	0	2 (2.5)
炎症	0	0	0	1 (8.3)	1 (1.3)
注射部位紅斑	0	1 (2.9)	1 (1.5)	0	1 (1.3)
注射部位炎症	1 (3.0)	0	1 (1.5)	0	1 (1.3)
注射部位浮腫	1 (3.0)	0	1 (1.5)	0	1 (1.3)
注射部位疼痛	1 (3.0)	0	1 (1.5)	0	1 (1.3)
注射部位そう痒感	0	1 (2.9)	1 (1.5)	0	1 (1.3)
注射部位腫脹	1 (3.0)	0	1 (1.5)	0	1 (1.3)
注射部位蕁麻疹	0	1 (2.9)	1 (1.5)	0	1 (1.3)
倦怠感	0	1 (2.9)	1 (1.5)	0	1 (1.3)
発熱	1 (3.0)	0	1 (1.5)	0	1 (1.3)
免疫系障害	0	1 (2.9)	1 (1.5)	0	1 (1.3)
薬物過敏症	0	1 (2.9)	1 (1.5)	0	1 (1.3)
感染症および寄生虫症	11 (33.3)	16 (45.7)	27 (39.7)	5 (41.7)	32 (40.0)
気管支炎	1 (3.0)	0	1 (1.5)	0	1 (1.3)
感染性腸炎	1 (3.0)	0	1 (1.5)	0	1 (1.3)
胃腸炎	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.8)
膿痂疹	0	1 (2.9)	1 (1.5)	0	1 (1.3)
感染性嚢腫	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 3. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
感染症および寄生虫症 (Cont.)					
インフルエンザ	0	2 (5.7)	2 (2.9)	0	2 (2.5)
喉頭炎	0	1 (2.9)	1 (1.5)	0	1 (1.3)
無菌性髄膜炎	0	1 (2.9)	1 (1.5)	0	1 (1.3)
上咽頭炎	3 (9.1)	4 (11.4)	7 (10.3)	1 (8.3)	8 (10.0)
口腔ヘルペス	0	1 (2.9)	1 (1.5)	0	1 (1.3)
中耳炎	0	1 (2.9)	1 (1.5)	0	1 (1.3)
咽頭炎	2 (6.1)	2 (5.7)	4 (5.9)	1 (8.3)	5 (6.3)
気道感染	1 (3.0)	0	1 (1.5)	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 (3.0)	0	1 (1.5)	0	1 (1.3)
癜風	1 (3.0)	0	1 (1.5)	0	1 (1.3)
歯膿瘍	0	0	0	1 (8.3)	1 (1.3)
気管炎	1 (3.0)	0	1 (1.5)	0	1 (1.3)
上気道感染	2 (6.1)	4 (11.4)	6 (8.8)	2 (16.7)	8 (10.0)
尿路感染	1 (3.0)	2 (5.7)	3 (4.4)	0	3 (3.8)
水痘	0	1 (2.9)	1 (1.5)	0	1 (1.3)
傷害、中毒および処置合併症	0	3 (8.6)	3 (4.4)	1 (8.3)	4 (5.0)
眼瞼挫傷	0	1 (2.9)	1 (1.5)	0	1 (1.3)
手骨折	0	2 (5.7)	2 (2.9)	0	2 (2.5)
関節損傷	0	0	0	1 (8.3)	1 (1.3)
靭帯捻挫	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 3. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
臨床検査	5 (15.2)	3 (8.6)	8 (11.8)	0	8 (10.0)
血中ビリルビン増加	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
血中カルシウム減少	1 (3.0)	0	1 (1.5)	0	1 (1.3)
血中ナトリウム減少	0	1 (2.9)	1 (1.5)	0	1 (1.3)
骨密度減少	1 (3.0)	0	1 (1.5)	0	1 (1.3)
C一反応性蛋白増加	3 (9.1)	0	3 (4.4)	0	3 (3.8)
好酸球数増加	0	1 (2.9)	1 (1.5)	0	1 (1.3)
リンパ節触知	1 (3.0)	0	1 (1.5)	0	1 (1.3)
結核菌群検査陽性	0	1 (2.9)	1 (1.5)	0	1 (1.3)
好中球数減少	1 (3.0)	0	1 (1.5)	0	1 (1.3)
白血球数減少	1 (3.0)	0	1 (1.5)	0	1 (1.3)
筋骨格系および結合組織障害	1 (3.0)	2 (5.7)	3 (4.4)	1 (8.3)	4 (5.0)
関節痛	0	1 (2.9)	1 (1.5)	0	1 (1.3)
背部痛	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
筋骨格痛	0	0	0	1 (8.3)	1 (1.3)
神経系障害	6 (18.2)	3 (8.6)	9 (13.2)	2 (16.7)	11 (13.8)
頭痛	6 (18.2)	2 (5.7)	8 (11.8)	2 (16.7)	10 (12.5)
感覚鈍麻	0	1 (2.9)	1 (1.5)	0	1 (1.3)
錯感覚	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 3. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
精神障害	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
うつ病	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
生殖系および乳房障害	0	1 (2.9)	1 (1.5)	0	1 (1.3)
月経困難症	0	1 (2.9)	1 (1.5)	0	1 (1.3)
呼吸器、胸郭および縦隔障害	4 (12.1)	5 (14.3)	9 (13.2)	3 (25.0)	12 (15.0)
喘息	1 (3.0)	0	1 (1.5)	0	1 (1.3)
咳嗽	0	2 (5.7)	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 (1.5)	0	1 (1.3)
口腔咽頭痛	2 (6.1)	1 (2.9)	3 (4.4)	0	3 (3.8)
アレルギー性鼻炎	0	2 (5.7)	2 (2.9)	0	2 (2.5)
鼻漏	1 (3.0)	0	1 (1.5)	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 (3.0)	7 (20.0)	8 (11.8)	3 (25.0)	11 (13.8)
脱毛症	0	1 (2.9)	1 (1.5)	0	1 (1.3)
皮膚炎	0	1 (2.9)	1 (1.5)	1 (8.3)	2 (2.5)
紅斑	0	1 (2.9)	1 (1.5)	0	1 (1.3)
結節性紅斑	0	1 (2.9)	1 (1.5)	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)

表 3. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
皮膚および皮下組織障害 (Cont.)					
紫斑	0	1 (2.9)	1 (1.5)	0	1 (1.3)
発疹	1 (3.0)	2 (5.7)	3 (4.4)	0	3 (3.8)
痂皮	0	1 (2.9)	1 (1.5)	0	1 (1.3)
脂漏	1 (3.0)	0	1 (1.5)	0	1 (1.3)
皮膚病変	0	1 (2.9)	1 (1.5)	0	1 (1.3)

One patient ([redacted]) who is ongoing study is excluded from interim analysis.
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.

相互参照：M11-290 日本サブ試験 中間 CSR Table 14.3__1.2.1.1.2_A

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）（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=3) n (%)	Total-ADA (N=5) n (%)	M-PL (N=0) n (%)	Total (N=5) n (%)
Any adverse event	1 (50.0)	3 (100)	4 (80.0)	0	4 (80.0)
感染症および寄生虫症	1 (50.0)	3 (100)	4 (80.0)	0	4 (80.0)
感染性腸炎	1 (50.0)	0	1 (20.0)	0	1 (20.0)
膿痂疹	0	1 (33.3)	1 (20.0)	0	1 (20.0)
インフルエンザ	0	1 (33.3)	1 (20.0)	0	1 (20.0)
上気道感染	0	1 (33.3)	1 (20.0)	0	1 (20.0)
傷害、中毒および処置合併症	0	2 (66.7)	2 (40.0)	0	2 (40.0)
眼瞼挫傷	0	1 (33.3)	1 (20.0)	0	1 (20.0)
手骨折	0	1 (33.3)	1 (20.0)	0	1 (20.0)
靭帯捻挫	0	1 (33.3)	1 (20.0)	0	1 (20.0)
皮膚および皮下組織障害	0	1 (33.3)	1 (20.0)	0	1 (20.0)
紫斑	0	1 (33.3)	1 (20.0)	0	1 (20.0)

One patient ([redacted]) who is ongoing study is excluded from interim analysis.
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.

相互参照：M11-290 日本サブ試験 中間 CSR Table 14.3__1.2.1.1.2_J

表 5. 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=17) n (%)	Total (N=100) n (%)
Any adverse event	19 (59.4)	27 (52.9)	13 (76.5)	59 (59.0)
No Reasonable Possibility	14 (43.8)	19 (37.3)	11 (64.7)	44 (44.0)
Reasonable Possibility	5 (15.6)	8 (15.7)	2 (11.8)	15 (15.0)
血液およびリンパ系障害	3 (9.4)	3 (5.9)	1 (5.9)	7 (7.0)
No Reasonable Possibility	3 (9.4)	3 (5.9)	1 (5.9)	7 (7.0)
貧血	3 (9.4)	3 (5.9)	1 (5.9)	7 (7.0)
No Reasonable Possibility	3 (9.4)	3 (5.9)	1 (5.9)	7 (7.0)
血小板増加症	0	0	1 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	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 5. 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=17) n (%)	Total (N=100) 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 (29.4)	20 (20.0)
No Reasonable Possibility	6 (18.8)	6 (11.8)	4 (23.5)	16 (16.0)
Reasonable Possibility	0	3 (5.9)	1 (5.9)	4 (4.0)
腹痛	0	2 (3.9)	2 (11.8)	4 (4.0)
No Reasonable Possibility	0	2 (3.9)	2 (11.8)	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 (5.9)	7 (7.0)
No Reasonable Possibility	4 (12.5)	2 (3.9)	0	6 (6.0)
Reasonable Possibility	0	0	1 (5.9)	1 (1.0)
便秘	0	0	1 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	1 (1.0)

表 5. 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=17) n (%)	Total (N=100) n (%)
胃腸障害 (Cont.)				
下痢	0	0	1 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	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 (5.9)	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	1 (5.9)	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 (5.9)	4 (4.0)
No Reasonable Possibility	0	2 (3.9)	1 (5.9)	3 (3.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)

表 5. 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=17) n (%)	Total (N=100) 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 (5.9)	2 (2.0)
No Reasonable Possibility	0	0	1 (5.9)	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)	0	12 (12.0)
No Reasonable Possibility	4 (12.5)	3 (5.9)	0	7 (7.0)
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 5. 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=17) n (%)	Total (N=100) 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	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
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 (35.3)	23 (23.0)
No Reasonable Possibility	6 (18.8)	11 (21.6)	5 (29.4)	22 (22.0)
Reasonable Possibility	0	0	1 (5.9)	1 (1.0)
気管支炎	0	0	1 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	1 (1.0)

表 5. 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=17) n (%)	Total (N=100) 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 (5.9)	5 (5.0)
No Reasonable Possibility	2 (6.3)	2 (3.9)	1 (5.9)	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 (5.9)	4 (4.0)
No Reasonable Possibility	2 (6.3)	1 (2.0)	1 (5.9)	4 (4.0)
レンサ球菌感染	0	0	1 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	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 5. 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=17) n (%)	Total (N=100) 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 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	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 (5.9)	1 (1.0)
Reasonable Possibility	0	0	1 (5.9)	1 (1.0)
傷害、中毒および処置合併症	4 (12.5)	2 (3.9)	0	6 (6.0)
No Reasonable Possibility	4 (12.5)	2 (3.9)	0	6 (6.0)
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 5. 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=17) n (%)	Total (N=100) 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 (11.8)	6 (6.0)
No Reasonable Possibility	2 (6.3)	1 (2.0)	1 (5.9)	4 (4.0)
Reasonable Possibility	0	1 (2.0)	1 (5.9)	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 5. 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=17) n (%)	Total (N=100) n (%)
臨床検査 (Cont.)				
肝酵素上昇	0	0	1 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	1 (1.0)
単球数減少	0	0	1 (5.9)	1 (1.0)
Reasonable Possibility	0	0	1 (5.9)	1 (1.0)
好中球数減少	0	0	1 (5.9)	1 (1.0)
Reasonable Possibility	0	0	1 (5.9)	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 (5.9)	1 (1.0)
Reasonable Possibility	0	0	1 (5.9)	1 (1.0)
筋骨格系および結合組織障害	2 (6.3)	2 (3.9)	1 (5.9)	5 (5.0)
No Reasonable Possibility	1 (3.1)	2 (3.9)	1 (5.9)	4 (4.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
関節痛	1 (3.1)	0	1 (5.9)	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	1 (5.9)	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 5. 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=17) n (%)	Total (N=100) n (%)
筋骨格系および結合組織障害 (Cont.)				
靭帯障害	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 (23.5)	15 (15.0)
No Reasonable Possibility	4 (12.5)	3 (5.9)	4 (23.5)	11 (11.0)
Reasonable Possibility	2 (6.3)	2 (3.9)	0	4 (4.0)
頭痛	5 (15.6)	5 (9.8)	4 (23.5)	14 (14.0)
No Reasonable Possibility	4 (12.5)	3 (5.9)	4 (23.5)	11 (11.0)
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 (5.9)	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	1 (5.9)	2 (2.0)

表 5. 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=17) n (%)	Total (N=100) n (%)
腎および尿路障害	0	0	1 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	1 (1.0)
糖尿	0	0	1 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	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 (17.6)	7 (7.0)
No Reasonable Possibility	1 (3.1)	3 (5.9)	3 (17.6)	7 (7.0)
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 (11.8)	4 (4.0)
No Reasonable Possibility	1 (3.1)	1 (2.0)	2 (11.8)	4 (4.0)

表 5. 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=17) n (%)	Total (N=100) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
鼻漏	0	1 (2.0)	1 (5.9)	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	1 (5.9)	2 (2.0)
皮膚および皮下組織障害	1 (3.1)	0	1 (5.9)	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	1 (5.9)	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 (5.9)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.9)	1 (1.0)

One patient ([redacted]) who is ongoing study is excluded from interim analysis.
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."

相互参照：M11-290 日本サブ試験 中間 CSR Table 14.3__1.3.1.1_A

表 6. 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=1) n (%)	Total (N=7) n (%)
Any adverse event	2 (100)	4 (100)	1 (100)	7 (100)
No Reasonable Possibility	1 (50.0)	3 (75.0)	0	4 (57.1)
Reasonable Possibility	1 (50.0)	1 (25.0)	1 (100)	3 (42.9)
眼障害	0	1 (25.0)	0	1 (14.3)
No Reasonable Possibility	0	1 (25.0)	0	1 (14.3)
眼瞼炎	0	1 (25.0)	0	1 (14.3)
No Reasonable Possibility	0	1 (25.0)	0	1 (14.3)
一般・全身障害および投与部位の状態	2 (100)	1 (25.0)	0	3 (42.9)
No Reasonable Possibility	1 (50.0)	0	0	1 (14.3)
Reasonable Possibility	1 (50.0)	1 (25.0)	0	2 (28.6)
異常感	1 (50.0)	0	0	1 (14.3)
No Reasonable Possibility	1 (50.0)	0	0	1 (14.3)
注射部位紅斑	0	1 (25.0)	0	1 (14.3)
Reasonable Possibility	0	1 (25.0)	0	1 (14.3)
注射部位疼痛	1 (50.0)	0	0	1 (14.3)
Reasonable Possibility	1 (50.0)	0	0	1 (14.3)
感染症および寄生虫症	0	3 (75.0)	0	3 (42.9)
No Reasonable Possibility	0	3 (75.0)	0	3 (42.9)

表 6. 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=1) n (%)	Total (N=7) n (%)
感染症および寄生虫症 (Cont.)				
外耳炎	0	1 (25.0)	0	1 (14.3)
No Reasonable Possibility	0	1 (25.0)	0	1 (14.3)
上気道感染	0	2 (50.0)	0	2 (28.6)
No Reasonable Possibility	0	2 (50.0)	0	2 (28.6)
臨床検査	0	0	1 (100)	1 (14.3)
Reasonable Possibility	0	0	1 (100)	1 (14.3)
単球数減少	0	0	1 (100)	1 (14.3)
Reasonable Possibility	0	0	1 (100)	1 (14.3)
好中球数減少	0	0	1 (100)	1 (14.3)
Reasonable Possibility	0	0	1 (100)	1 (14.3)
白血球数減少	0	0	1 (100)	1 (14.3)
Reasonable Possibility	0	0	1 (100)	1 (14.3)
神経系障害	1 (50.0)	0	0	1 (14.3)
No Reasonable Possibility	1 (50.0)	0	0	1 (14.3)
頭痛	1 (50.0)	0	0	1 (14.3)
No Reasonable Possibility	1 (50.0)	0	0	1 (14.3)

表 6. 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）

One patient ([redacted] who is ongoing study is excluded from interim analysis.
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."

相互参照：M11-290 日本サブ試験 中間 CSR Table 14.3__1.3.1.1_J

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
Any adverse event	21 (63.6)	25 (71.4)	46 (67.6)	10 (83.3)	56 (70.0)
No Reasonable Possibility	13 (39.4)	14 (40.0)	27 (39.7)	5 (41.7)	32 (40.0)
Reasonable Possibility	8 (24.2)	11 (31.4)	19 (27.9)	5 (41.7)	24 (30.0)
血液およびリンパ系障害	4 (12.1)	1 (2.9)	5 (7.4)	2 (16.7)	7 (8.8)
No Reasonable Possibility	3 (9.1)	1 (2.9)	4 (5.9)	0	4 (5.0)
Reasonable Possibility	1 (3.0)	0	1 (1.5)	2 (16.7)	3 (3.8)
貧血	3 (9.1)	1 (2.9)	4 (5.9)	1 (8.3)	5 (6.3)
No Reasonable Possibility	2 (6.1)	1 (2.9)	3 (4.4)	0	3 (3.8)
Reasonable Possibility	1 (3.0)	0	1 (1.5)	1 (8.3)	2 (2.5)
リンパ節症	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	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 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
耳痛	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	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 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) 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 (27.3)	10 (28.6)	19 (27.9)	3 (25.0)	22 (27.5)
No Reasonable Possibility	7 (21.2)	7 (20.0)	14 (20.6)	3 (25.0)	17 (21.3)
Reasonable Possibility	2 (6.1)	3 (8.6)	5 (7.4)	0	5 (6.3)
腹痛	1 (3.0)	1 (2.9)	2 (2.9)	1 (8.3)	3 (3.8)
No Reasonable Possibility	1 (3.0)	1 (2.9)	2 (2.9)	1 (8.3)	3 (3.8)
上腹部痛	0	2 (5.7)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.7)	2 (2.9)	0	2 (2.5)
アフタ性潰瘍	1 (3.0)	0	1 (1.5)	0	1 (1.3)
Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
潰瘍性大腸炎	6 (18.2)	4 (11.4)	10 (14.7)	2 (16.7)	12 (15.0)
No Reasonable Possibility	5 (15.2)	2 (5.7)	7 (10.3)	2 (16.7)	9 (11.3)
Reasonable Possibility	1 (3.0)	2 (5.7)	3 (4.4)	0	3 (3.8)
便秘	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
下痢	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
胃腸障害 (Cont.)					
消化不良	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
小腸炎	2 (6.1)	1 (2.9)	3 (4.4)	0	3 (3.8)
No Reasonable Possibility	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
胃食道逆流性疾患	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
一般・全身障害および投与部位の状態	5 (15.2)	3 (8.6)	8 (11.8)	1 (8.3)	9 (11.3)
No Reasonable Possibility	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
Reasonable Possibility	4 (12.1)	2 (5.7)	6 (8.8)	1 (8.3)	7 (8.8)
胸痛	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
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 (1.3)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
注射部位紅斑	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) 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 (1.5)	0	1 (1.3)
Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
注射部位浮腫	1 (3.0)	0	1 (1.5)	0	1 (1.3)
Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
注射部位疼痛	1 (3.0)	0	1 (1.5)	0	1 (1.3)
Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
注射部位そう痒感	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
注射部位腫脹	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
注射部位蕁麻疹	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
倦怠感	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
発熱	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
免疫系障害	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
薬物過敏症	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
感染症および寄生虫症	11 (33.3)	16 (45.7)	27 (39.7)	5 (41.7)	32 (40.0)
No Reasonable Possibility	11 (33.3)	14 (40.0)	25 (36.8)	5 (41.7)	30 (37.5)
Reasonable Possibility	0	2 (5.7)	2 (2.9)	0	2 (2.5)
気管支炎	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
感染性腸炎	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
胃腸炎	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.8)
No Reasonable Possibility	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.8)
膿痂疹	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
感染性嚢腫	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
感染症および寄生虫症 (Cont.)					
インフルエンザ	0	2 (5.7)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
喉頭炎	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
無菌性髄膜炎	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
上咽頭炎	3 (9.1)	4 (11.4)	7 (10.3)	1 (8.3)	8 (10.0)
No Reasonable Possibility	3 (9.1)	4 (11.4)	7 (10.3)	1 (8.3)	8 (10.0)
口腔ヘルペス	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
中耳炎	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
咽頭炎	2 (6.1)	2 (5.7)	4 (5.9)	1 (8.3)	5 (6.3)
No Reasonable Possibility	2 (6.1)	2 (5.7)	4 (5.9)	1 (8.3)	5 (6.3)
気道感染	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
感染症および寄生虫症 (Cont.)					
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 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
癜風	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	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 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
上気道感染	2 (6.1)	4 (11.4)	6 (8.8)	2 (16.7)	8 (10.0)
No Reasonable Possibility	2 (6.1)	4 (11.4)	6 (8.8)	2 (16.7)	8 (10.0)
尿路感染	1 (3.0)	2 (5.7)	3 (4.4)	0	3 (3.8)
No Reasonable Possibility	1 (3.0)	2 (5.7)	3 (4.4)	0	3 (3.8)
水痘	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
傷害、中毒および処置合併症	0	3 (8.6)	3 (4.4)	1 (8.3)	4 (5.0)
No Reasonable Possibility	0	3 (8.6)	3 (4.4)	1 (8.3)	4 (5.0)
眼瞼挫傷	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
手骨折	0	2 (5.7)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.7)	2 (2.9)	0	2 (2.5)
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)
靭帯捻挫	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
臨床検査	5 (15.2)	3 (8.6)	8 (11.8)	0	8 (10.0)
No Reasonable Possibility	4 (12.1)	1 (2.9)	5 (7.4)	0	5 (6.3)
Reasonable Possibility	1 (3.0)	2 (5.7)	3 (4.4)	0	3 (3.8)
血中ビリルビン増加	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
血中カルシウム減少	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
臨床検査 (Cont.)					
血中ナトリウム減少	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
骨密度減少	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
C－反応性蛋白増加	3 (9.1)	0	3 (4.4)	0	3 (3.8)
No Reasonable Possibility	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
好酸球数増加	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
リンパ節触知	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
結核菌群検査陽性	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
好中球数減少	1 (3.0)	0	1 (1.5)	0	1 (1.3)
Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
白血球数減少	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
筋骨格系および結合組織障害	1 (3.0)	2 (5.7)	3 (4.4)	1 (8.3)	4 (5.0)
No Reasonable Possibility	1 (3.0)	1 (2.9)	2 (2.9)	1 (8.3)	3 (3.8)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
関節痛	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
背部痛	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
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)
神経系障害	6 (18.2)	3 (8.6)	9 (13.2)	2 (16.7)	11 (13.8)
No Reasonable Possibility	4 (12.1)	2 (5.7)	6 (8.8)	1 (8.3)	7 (8.8)
Reasonable Possibility	2 (6.1)	1 (2.9)	3 (4.4)	1 (8.3)	4 (5.0)
頭痛	6 (18.2)	2 (5.7)	8 (11.8)	2 (16.7)	10 (12.5)
No Reasonable Possibility	4 (12.1)	2 (5.7)	6 (8.8)	1 (8.3)	7 (8.8)
Reasonable Possibility	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.8)
感覚鈍麻	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
錯感覚	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
精神障害	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
うつ病	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	1 (2.9)	2 (2.9)	0	2 (2.5)
生殖系および乳房障害	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
月経困難症	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
呼吸器、胸郭および縦隔障害	4 (12.1)	5 (14.3)	9 (13.2)	3 (25.0)	12 (15.0)
No Reasonable Possibility	4 (12.1)	5 (14.3)	9 (13.2)	3 (25.0)	12 (15.0)
喘息	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
咳嗽	0	2 (5.7)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.7)	2 (2.9)	0	2 (2.5)
鼻出血	0	0	0	2 (16.7)	2 (2.5)
No Reasonable Possibility	0	0	0	2 (16.7)	2 (2.5)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
鼻浮腫	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
口腔咽頭痛	2 (6.1)	1 (2.9)	3 (4.4)	0	3 (3.8)
No Reasonable Possibility	2 (6.1)	1 (2.9)	3 (4.4)	0	3 (3.8)
アレルギー性鼻炎	0	2 (5.7)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.7)	2 (2.9)	0	2 (2.5)
鼻漏	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
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 (3.0)	7 (20.0)	8 (11.8)	3 (25.0)	11 (13.8)
No Reasonable Possibility	1 (3.0)	2 (5.7)	3 (4.4)	1 (8.3)	4 (5.0)
Reasonable Possibility	0	5 (14.3)	5 (7.4)	2 (16.7)	7 (8.8)
脱毛症	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
皮膚炎	0	1 (2.9)	1 (1.5)	1 (8.3)	2 (2.5)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
皮膚および皮下組織障害 (Cont.)					
紅斑	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
結節性紅斑	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	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)
紫斑	0	1 (2.9)	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
発疹	1 (3.0)	2 (5.7)	3 (4.4)	0	3 (3.8)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)
Reasonable Possibility	0	2 (5.7)	2 (2.9)	0	2 (2.5)
痂皮	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)
脂漏	1 (3.0)	0	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	1 (3.0)	0	1 (1.5)	0	1 (1.3)

表 7. 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=35) n (%)	Total-ADA (N=68) n (%)	M-PL (N=12) n (%)	Total (N=80) n (%)
皮膚および皮下組織障害 (Cont.)					
皮膚病変	0	1 (2.9)	1 (1.5)	0	1 (1.3)
No Reasonable Possibility	0	1 (2.9)	1 (1.5)	0	1 (1.3)

One patient ([redacted]) who is ongoing study is excluded from interim analysis.
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."

相互参照：M11-290 日本サブ試験 中間 CSR Table 14.3__1.3.1.2_A

表 8. 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=3) n (%)	Total-ADA (N=5) n (%)	M-PL (N=0) n (%)	Total (N=5) n (%)
Any adverse event	1 (50.0)	3 (100)	4 (80.0)	0	4 (80.0)
No Reasonable Possibility	1 (50.0)	2 (66.7)	3 (60.0)	0	3 (60.0)
Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)
感染症および寄生虫症	1 (50.0)	3 (100)	4 (80.0)	0	4 (80.0)
No Reasonable Possibility	1 (50.0)	2 (66.7)	3 (60.0)	0	3 (60.0)
Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)
感染性腸炎	1 (50.0)	0	1 (20.0)	0	1 (20.0)
No Reasonable Possibility	1 (50.0)	0	1 (20.0)	0	1 (20.0)
膿痂疹	0	1 (33.3)	1 (20.0)	0	1 (20.0)
No Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)
インフルエンザ	0	1 (33.3)	1 (20.0)	0	1 (20.0)
Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)
上気道感染	0	1 (33.3)	1 (20.0)	0	1 (20.0)
No Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)
傷害、中毒および処置合併症	0	2 (66.7)	2 (40.0)	0	2 (40.0)
No Reasonable Possibility	0	2 (66.7)	2 (40.0)	0	2 (40.0)
眼瞼挫傷	0	1 (33.3)	1 (20.0)	0	1 (20.0)
No Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)

表 8. 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=3) n (%)	Total-ADA (N=5) n (%)	M-PL (N=0) n (%)	Total (N=5) n (%)
傷害、中毒および処置合併症 (Cont.)					
手骨折	0	1 (33.3)	1 (20.0)	0	1 (20.0)
No Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)
靭帯捻挫	0	1 (33.3)	1 (20.0)	0	1 (20.0)
No Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)
皮膚および皮下組織障害	0	1 (33.3)	1 (20.0)	0	1 (20.0)
Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)
紫斑	0	1 (33.3)	1 (20.0)	0	1 (20.0)
Reasonable Possibility	0	1 (33.3)	1 (20.0)	0	1 (20.0)

One patient ([redacted]) who is ongoing study is excluded from interim analysis.
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."

相互参照：M11-290 日本サブ試験 中間 CSR 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
MULTIVITAMIN	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
MULTIVITAMIN	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

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
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]
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] /

			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] / 62	Y-M: 20[redacted] / 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): CEREBRAL SPINAL FLUID BACTERIAL CULTURE: NEGATIVE; URINE CULTURE: NEGATIVE; BLOOD CULTURES: NEGATIVE; THROAT CULTURE: NO GROUP A BETA STREP; LUMBAR PUNCTURE: 52 NUCLEATED CELLS, 48% PMN, 47% LYMPH, 38 PROTEIN AND 60 GLUCOSE.; HEAD CT: NORMAL UNENHANCED CT OF THE HEAD; [redacted]20[redacted] (RX DAY 65): BRAIN MRI: NORMAL MRI OF THE BRAIN WITH INTRAVENOUS CONTRAST; BRAIN MRV: NORMAL INTRACRANIAL MR VENOGRAM

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]: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（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

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]: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（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]

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
SUCRALFATE	1 g (gram(s))	TID	Y-M: 20[redacted]-[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
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]: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（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
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] Y-M: 20[redacted] / / 47 51
FLEET	133 mL (millilitre(s))	PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 47 56
SENNA ALEXANDRINA	8.6 mg (milligram(s))	PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 47 56
MORPHINE	5 mg (milligram(s))	PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 49 49
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 49 55
IBUPROFEN	221 mg (milligram(s))	PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 56 56
METRONIDAZOLE	500 mg (milligram(s))	OTHER: Q8 HOURS	Y-M: 20[redacted] Y-M: 20[redacted] / / 56 56
HYDROCORTISONE	33 mg (milligram(s))	OTHER: Q8 HOURS	Y-M: 20[redacted] Y-M: 20[redacted] / / 56 57
CEFTRIAXONE	2000 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 56 62
DIMENHYDRINATE	25 mg (milligram(s))	PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 56 62
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 56 62
MORPHINE	3 mg (milligram(s))	PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 58 58
KETOROLAC	15 mg (milligram(s))	PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 58 59
FLEBOBAG RING LACT	500 mL (millilitre(s))	OTHER: ONCE	Y-M: 20[redacted] Y-M: 20[redacted] / / 59 59
HYDROCORTISONE	33 mg (milligram(s))	TID	Y-M: 20[redacted] Y-M: 20[redacted] / / 59 60
HYDROCORTISONE	17 mg (milligram(s))	TID	Y-M: 20[redacted] Y-M: 20[redacted] / / 61 62
HYDROCORTISONE	8 mg (milligram(s))	TID	Y-M: 20[redacted] Y-M: 20[redacted] / / 61 62
AMOXICILLIN W/CLAVULANATE POTASSIUM	1 TABLET	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] Y-M: 20[redacted] / / 62 67

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]: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（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

PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 65 / 71
PREDNISONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 72 / 78
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 78 / 85
METAMIZOLE SODIUM	500 mg (milligram(s))	OTHER: IN CASE OF FEVER	Y-M: 20[redacted]-Y-M: 20[redacted] / 85 / 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]-Y-M: 20[redacted] / 85 / 87
CIPROFLOXACIN	400 mg (milligram(s))	BID	Y-M: 20[redacted]-Y-M: 20[redacted] / 85 / 94
METRONIDAZOLE	350 mg (milligram(s))	TID	Y-M: 20[redacted]-Y-M: 20[redacted] / 85 / 94
PREDNISONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 86 / 92
FERRIC CARBOXYMALTOSE	500 mg (milligram(s))	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 91 / 91
CIPROFLOXACIN HYDROCHLORIDE	500 mg (milligram(s))	BID	Y-M: 20[redacted]-Y-M: 20[redacted] / 95 / 102
METRONIDAZOLE	250 mg (milligram(s))	TID	Y-M: 20[redacted]-Y-M: 20[redacted] / 95 / 108
SODIUM CHLORIDE	500 mL (millilitre(s))	OTHER: ACCORDING TO FLUID BALANCE	Y-M: 20[redacted]-Y-M: 20[redacted] / 112 / 113
OMEPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 113 / 113
ELECTROLYTES NOS W/GLUCOSE	500 mL (millilitre(s))	OTHER: ACCORDING TO BALANCE OF FLUID AND IONS LEVEL	Y-M: 20[redacted]-Y-M: 20[redacted] / 113 / 115
BLOOD AND RELATED PRODUCTS	1 TU	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 128 / 129
AMINO ACIDS NOS W/ELECTROLYTES NOS/	1000 mL (millilitre(s))	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 129 / 135
FERRIC CARBOXYMALTOSE	500 mg (milligram(s))	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 132 / 132
METHYLPREDNISOLONE SODIUM SUCCINATE	500 mg (milligram(s))	QD	Y-M: 20[redacted]-Y-M: 20[redacted] / 133 / 135
POTASSIUM CHLORIDE	600 mg (milligram(s))	QD	Y-M: 20[redacted]-ONGOING / 134
PREDNISONE	60 mg (milligram(s))	QD	Y-M: 20[redacted]-ONGOING / 136

ALPRAZOLAM	0.25 mg (milligram(s))	OTHER: 1/2-1/2-1	Y-M: 20[redacted]-ONGOING [redacted] / 139

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]: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（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
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] 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

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]: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