Interruption				[redacted]20[redacted] / 105	[redacted]20[redacted] / 112	8
Risankizumab	360 mg	SC	Every 8 Weeks	[redacted]20[redacted] / 113	[redacted]20[redacted] / 152	40

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BUDESONIDE	3 mg	TID	Y-M: 20[redacted]
METHYLPREDNISOLONE	32 mg	OTHER: UNKNOWN	Y-M: 20[redacted]
MESALAZINE	1 g	TID	Y-M: 20[redacted]
METHYLPREDNISOLONE	32 mg	OTHER: UNKNOWN	Y-M: 20[redacted]
BUDESONIDE	3 mg	TID	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: 1 TIME PER 2 WEEKS	Y-M: 20[redacted] / -165
ADALIMUMAB	40 mg	OTHER: ONE TIME PER 2 WEEKS	Y-M: 20[redacted] / -150

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
BUDESONIDE	3 mg	TID	Y-M: 20[redacted]	ONGOING
PARACETAMOL	1000 mg	OTHER: ONE TIME PER DAY	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 91
BARALGINA	2 mL	OTHER: ONE TIME EVERY DAY	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 92
DEXKETOPROFEN	50 mg	OTHER: ONE TIME PER DAY	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 92
CEFTRIAXONE	1000 mg	BID	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 98
SULBACTAM	500 mg	BID	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 98
CEFIXIME	400 mg	OTHER: ONCE TIME PER DAY	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 103

Event #1: Serious Adverse Event

Event Description CALCULUS OF RIGHT URETER

Preferred term 尿管結石症

AE Onset Date / Rx Day [redacted]20[redacted] / 88

Age at AE Onset 2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 88): Bilirubin: 12.4 [5 - 21] umol/L; Blood Urea Nitrogen: 5.2 [2.1 - 7.1] mmol/L; Creatinine: 0.098 [0.053 - 0.097] mmol/L; Erythrocytes: 4.6 [3.8 - 5.1] 10^12/L; Hemoglobin: 133 [117 - 155] g/L; Leukocytes: 13.7 [4.5 - 11] 10^9/L; Protein: 76.9 [64 - 83] g/L

Microbiology

Not reported

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 87): CT SCAN OF THE ABDOMINAL CAVITY, RETROPERITONEAL SPACE, PELVIS: URETERAL STONE WAS VISUALIZED; LITHOTRIPSY: DESTRUCTED URETERAL STONE; ULTRASOUND OF THE RETROPERITONEAL SPACE: URETERAL STONE WAS VISUALIZED

AE Stopped Rx Day	98
Duration of AE	11 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	UROLITHIASIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

ウクライナの治験責任医師からの報告。本被験者は2[redacted]歳女性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，右尿管結石の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，非喫煙者及び非飲酒者であった。

投与 88 日後，被験者は右尿管結石を発現した。投与 98 日後，右尿管結石は消失した。

投与 88 日後，被験者は右腰部の疼痛，悪心，嘔吐及び脱力を訴え入院した。投与 89 日後，被験者は砕石を受けた。処置により尿管結石の破砕は成功した。被験者に改善が認められた。投与 98 日後，被験者は満足できる状態で退院した。

投与された薬剤は，セフトリアキソン（セフトリアキソンナトリウム），スルバクタム（スルバクタムナトリウム），セフィキシム，Dexalgin，Spasmalgon，Uroclin 及び paracetamol であった。

The patient's past medications include:

METHYLPREDNISOLONE for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - 20[redacted])

MESALAZINE for CROHN'S DISEASE ([redacted] 20[redacted] - 20[redacted])

HUMIRA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Calculus of ureter (10007018) (Ureterolithiasis (10077989)) [v.23.1] [10007018]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of CALCULUS OF RIGHT URETER

- Investigator: Urolithiasis

- AbbVie: Renal stone is a relatively common problem with an estimated 8 percent of women who will be diagnosed with a kidney stone by age of 70 years. In addition, pre-existing Crohn's disease, particularly in those patients who have had bowel surgery, is a significant risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BILIRUBIN: 12.4 umol/L

[redacted] 20[redacted] BUN: 5.2 MMOL/L

[redacted] 20[redacted] CREATININE: 0.098 MMOL/L

[redacted] 20[redacted] CT SCAN OF THE ABDOMINAL CAVITY, RETROPERITONEAL SPACE, PELVIS: URETERAL STONE WAS VISUALIZED

[redacted] 20[redacted] HEMOGLOBIN: 133 G/L

[redacted] 20[redacted] PROTEIN: 76.9 G/L

[redacted] 20[redacted] RED BLOOD CELLS: 4.6 10^12/L

[redacted] 20[redacted] ULTRASOUND OF THE RETROPERITONEAL SPACE: URETERAL STONE WAS VISUALIZED

[redacted] 20[redacted] WHITE BLOOD CELLS: 13.7 10^9/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
イレウス	X			

Treatment Group	Age at Study Start	Sex	Race
P1:RZB 600 MG IV / P2:RZB 360 mg SC	4[redacted]	MALE	ASIAN

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: POLLINOSIS	20[redacted]
OTHER: ANAL BOUGIE	20[redacted]
OTHER: MILIARIA	20[redacted]
OTHER: STOMATITIS	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: ANAL BOUGIE	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BALLOON DILATATION	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
Risankizumab	360 mg	SC	Every 8 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 141	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
CARBOHYDRATES NOS W/ELECTROLYTES NOS/LIPIDS N	400 OTHER: KCAL	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg	TID	Y-M: 20[redacted]
INFLIXIMAB	UNK OTHER: UNK	QD	Y-M: 20[redacted]
AMINO ACIDS NOS W/CARBOHYDRATES NOS	300 OTHER: KCAL	BID	Y-M: 20[redacted]
INFLIXIMAB	260 mg	OTHER: TIME PER 2-4WEEKS	Y-M: 20[redacted]
AMINO ACIDS NOS W/CARBOHYDRATES NOS	300 OTHER: KCAL	TID	Y-M: 20[redacted]
AMINO ACIDS NOS W/CARBOHYDRATES NOS	300 OTHER: KCAL	BID	Y-M: 20[redacted]
INFLIXIMAB	300 mg	OTHER: TIME PER 2WEEKS	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
ADALIMUMAB	160 mg	OTHER: TIME PER 2WEEKS	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: 1TIME PER 2WEEKS	Y-M: 20[redacted]
MESALAZINE	0.5 g	QD	Y-M: 20[redacted]
PREDNISOLONE	30 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	75 mg	QD	Y-M: 20[redacted]
CIPROFLOXACIN	200 mg	BID	Y-M: 20[redacted]
SULFASALAZINE	500 mg	TID	Y-M: 20[redacted] / -245
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -111
AMINO ACIDS NOS W/CARBOHYDRATES NOS	300 OTHER: KCAL	QD	Y-M: 20[redacted] / -84
BILASTINE	20 mg	QD	Y-M: 20[redacted] / -21
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -21
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / -21
SODIUM PICOSULFATE	10 mL	PRN	Y-M: 20[redacted] / -8
COLYTE	2 L	PRN	Y-M: 20[redacted] / -7
LIDOCAINE	15 mL	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
AMINO ACIDS NOS W/CARBOHYDRATES NOS	300 OTHER: KCAL	QD	Y-M: 20[redacted] / -84	ONGOING
RESTAMIN A KOWA	50 mg	OTHER: 1 TIME PER 4WEEKS	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 141

IOPAMIDOL	100 mL	PRN	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 79
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 79
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 82
OSMOSAL	500 mL	QID	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 87
SODIUM PICOSULFATE	10 mL	PRN	Y-M: 20[redacted]-[redacted] / 84	Y-M: 20[redacted]-[redacted] / 84
COLYTE	2 L	PRN	Y-M: 20[redacted]-[redacted] / 85	Y-M: 20[redacted]-[redacted] / 85
LIDOCAINE	15 mL	PRN	Y-M: 20[redacted]-[redacted] / 85	Y-M: 20[redacted]-[redacted] / 85

Event #1: Serious Adverse Event

Event Description	ILEUS OF SMALL INTESTINE
Preferred term	イレウス
AE Onset Date / Rx Day	[redacted]20[redacted] / 78
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 79): Leukocytes: 18.3 [5 - 8] 10^3/uL; NPTST050-C REACTIVE PROTEIN: 1.94 [0 - 0.3] mg/dL

Microbiology

[redacted]20[redacted] (Rx Day 79): STOOL NPTST073-CULTURE TEST: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 65): ABDOMINAL X-RAY EXAMINATION: IT WAS ILLUSTRATED THE CONDITION IMPROVING.; ABDOMINAL X-RAY EXAMINATION: THE GAS IN THE SMALL INTESTINE TO HAVE DISAPPEARED.; CHEST AND ABDOMINAL X-RAY EXAMINATION: DILATATION AND FLUID RETENTION IN THE SMALL INTESTINE WERE ILLUSTRATED.; COLONOSCOPY: LONGITUDINAL ULCER IS OBSERVED, BUT THE WIDTH IS NARROWER THAN THE PREVIOUS EXAMINATION ([redacted]/[redacted]/20[redacted]). THE INNER DEAMETER OF ILEUM IS A LITTLE NARROW.; CT SCAN: DILATATION AND FLUID RETENTION IN THE SMALL INTESTINE WERE ILLUSTRATED.

AE Stopped Rx Day	88
Duration of AE	11 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	THE HISTORY OF REPEATED ILEUS BEFORE THIS STUDY.RECENT OVEREATING.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

日本の治験責任医師からの報告。本被験者は4[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，小腸のイレウスの事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，イレウス，腸切除，肛門ブジー，非喫煙者及び飲酒者（1 日 2 杯未満）であった。

投与 78 日後，被験者は小腸のイレウスを発現した。投与 88 日後，小腸のイレウスは消失した。

本事象発現前の投与 60 日後，被験者は便秘（非重篤）を発現した。

投与 78 日後の朝，下腹部痛が始まった。疼痛が増悪し，被験者は嘔吐した。投与 79 日後，被験者は病院に救急搬送され，入院した。被験者は絶食となり，薬剤の投与を受けた。被験者は多量の便を排泄した。午後，悪心は消失した。腹部症状が改善し始めた。投与 83 日後，腹痛は不快感の程度まで改善し，腹部は平坦で軟らかく，圧痛はなかった。内視鏡検査の結果から被験者の状態は良好と判断され，食事が再開された。腹痛の訴えはなく，便通は良好であった。投与 88 日後，被験者は退院した。

投与された薬剤は，ソリタ-T，セフトリアキソンナトリウム及びアセリオであった。

The patient’s past medications include:

PREDONINE for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted], [redacted]20[redacted] - [redacted]20[redacted])

PENTASA for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted])

RACOL-NF LIQUID for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted])

REMICADE for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted], [redacted]20[redacted] - [redacted]20[redacted], [redacted]20[redacted] - [redacted]20[redacted])

PENTASA SUPPOSITORIES for CROHN'S DISEASE ([redacted] 20[redacted] - 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

IMURAN for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

CIPROFLOXACIN for ANAL FISTULA ([redacted] 20[redacted] - [redacted] 20[redacted])

SALAZOPYRIN for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

ZENTACORT for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Ileus of intestine (10021332) (Ileus (10021328)) [v.22.0] [10021332]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of ILEUS OF SMALL INTESTINE

- Investigator: The history of repeated ileus before this study. Recent overeating..

- AbbVie: Risk factors include pre-existing Crohn's disease and history of pre-existing episodes of ileus.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL X-RAY:** Dilatation and fluid retention in the small intestine were illustrated. Ileus of small intestine was diagnosed.

[redacted] **20[redacted] ABDOMINAL X-RAY:** Revealed the gas in the small intestine to have disappeared. Inflammatory reaction improved.

[redacted] **20[redacted] CHEST AND ABDOMINAL XRAY:** Dilatation and fluid retention in the small intestine were illustrated.

[redacted] **20[redacted] CHEST X-RAY:** Results not reported

[redacted] **20[redacted] CRP:** 1.94 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CT SCAN:** Dilatation and fluid retention in the small intestine were illustrated. Ileus of small intestine was diagnosed.

[redacted] **20[redacted] ENDOSCOPY:** Longitudinal ulcer was observed in the ileum from the anastomotic site, and the lumen seemed to have been narrowed compared with it at the study initiation.

[redacted] 20[redacted] STOOL CULTURE: Negative

[redacted] **20[redacted] WBC:** 18.3 X10**3/MCL (normal 5.0 to 8.0)

[redacted] 20[redacted] WEIGHT: 7[redacted].[redacted] KG

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
クローン病	X			

Treatment Group	Age at Study Start	Sex	Race
P1:RZB 600 MG IV	3[redacted]	MALE	ASIAN

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: DRY SKIN	20[redacted]
OTHER: POMPHOLYX ECZEMA	20[redacted]
OTHER: ACNE VULGARIS	20[redacted]
ANEMIA: IRON DEFICIENCY ANAEMIA	20[redacted]
OTHER: FOLLICULITIS	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF PELVIC ABSCESS	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: PLACEMENTS OF SETONS	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: STRICTUREPLASTY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF PERINEAL ABSCESS	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF PERINEAL ABSCESS	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: STRICTUREPLASTY	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): BIOPSY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted]
BCG Vaccine	Not reported.	Not reported.	Y-M: 20[redacted]
INFLIXIMAB	280 mg	OTHER: UNK	Y-M: 20[redacted]
INFLIXIMAB	UNKNOWN mg	OTHER: UNK	Y-M: 20[redacted]
ADALIMUMAB	160 mg	OTHER: ONCE EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: ONCE EVERY 2 WEEKS	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
HEPARINOID	PROPERDOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]
CLOBETASOL	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]
BETAMETHASONE	PROPERDPSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]
ECABET	1.5 g	BID	Y-M: 20[redacted]
BEPOTASTINE	20 mg	BID	Y-M: 20[redacted]
MESALAZINE	1000 mg	TID	Y-M: 20[redacted]
CLOBETASOL	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]
INFLIXIMAB	UNKNOWN mg	OTHER: WEEK0,2,6	Y-M: 20[redacted]
INFLIXIMAB	600 mg	OTHER: ONCE EVERY 8 WEEKS	Y-M: 20[redacted]
BENZOYL PEROXIDE	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
USTEKINUMAB	390 mg	OTHER: ONCE	Y-M: 20[redacted]
USTEKINUMAB	90 mg	OTHER: ONCE EVERY 8 WEEKS	Y-M: 20[redacted]
WHITE SOFT PARAFFIN	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]

CROTAMITON	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]
CARBOHYDRATES NOS W/ELECTROLYTES NOS/LIPIDS N	400 mL	PRN	Y-M: 20[redacted] / -217
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / -84
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -42
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -28
FLUMAZENIL	2.5 mL	OTHER: ONCE	Y-M: 20[redacted] / -21
LIDOCAINE	PROPER QUANITY OTHER: PROPER QUANITY	OTHER: ONCE	Y-M: 20[redacted] / -21
MIDAZOLAM	15 mL	OTHER: ONCE	Y-M: 20[redacted] / -21
MOVIPREP	2000 mL	OTHER: ONCE	Y-M: 20[redacted] / -21
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -21
RINGER-LACTATE	500 mL	OTHER: ONCE	Y-M: 20[redacted] / -21
SIMETICONE	10 mL	OTHER: ONCE	Y-M: 20[redacted] / -21
TIMEPIDIUM	1 mL	OTHER: ONCE	Y-M: 20[redacted] / -21
BEPOTASTINE	20 mg	BID	Y-M: 20[redacted] / -20
ECABET	1.5 g	BID	Y-M: 20[redacted] / -20
FAMOTIDINE	10 mg	BID	Y-M: 20[redacted] / -20
MESALAZINE	1000 mg	TID	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
BCG Vaccine	Not reported.	Not reported.	Y-M: 20[redacted]	Not reported.
HEPARINOID	PROPERDOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING
CLOBETASOL	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING
BETAMETHASONE	PROPERDPSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING
CLOBETASOL	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING
BENZOYL PEROXIDE	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING
WHITE SOFT PARAFFIN	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING

CROTAMITON	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING
CARBOHYDRATES NOS W/ELECTROLYTES NOS/LIPIDS N	400 mL	PRN	Y-M: 20[redacted] / - 217	ONGOING
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / - 21	Y-M: 20[redacted] / 85
BEPOTASTINE	20 mg	BID	Y-M: 20[redacted] / - 20	ONGOING
ECABET	1.5 g	BID	Y-M: 20[redacted] / - 20	ONGOING
FAMOTIDINE	10 mg	BID	Y-M: 20[redacted] / - 20	ONGOING
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / - 20	ONGOING
IOPAMIDOL	100 mL	OTHER: ONCE	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 16
METHYLPREDNISOLONE	500 mg	QD	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 23
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mg	TID	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 32
FLUMAZENIL	5 mL	OTHER: ONCE	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 29
LIDOCAINE	PROPER QUANTITY OTHER: PROPER QUANTITY	OTHER: ONCE	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 29
MAGNESIUM CITRATE	100 g	OTHER: ONCE	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 29
MIDAZOLAM	15 mL	OTHER: ONCE	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 29
SODIUM PICOSULFATE	10 mL	OTHER: ONCE	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 29
TIMEPIDIUM	1 mL	OTHER: ONCE	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 29
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	BID	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 33
HEPARIN	10 mL	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 33
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
FLUMAZENIL	2.5 mL	OTHER: ONCE	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 78

LIDOCAINE	PROPER QUANTITY OTHER: PROPER QUANTITY	OTHER: ONCE	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 78
MIDAZOLAM	15 mL	OTHER: ONCE	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 78
MOVIPREP	2000 mL	OTHER: ONCE	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 78
RINGER-LACTATE	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 78
SIMETICONE	10 mL	OTHER: ONCE	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 78
TIMEPIDIUM	1 mL	OTHER: ONCE	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 78

Event #1: Serious Adverse Event

Event Description	WORSENING OF CROHN'S DISEASE
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 13
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 28): NPTST070-CRP: 0.48 [0 - 0.14] mg/dL; [redacted]20[redacted] (Rx Day 31): NPTST070-CRP: 0.93 [0 - 0.14] mg/dL; [redacted]20[redacted] (Rx Day 34): NPTST070-CRP: 0.59 [0 - 0.14] mg/dL

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 8): ABDOMINAL ULTRASOUND: ANASTOMOSIS ULCER SIGMOID SOLON WALL THICHENING; COLONOSCOPY: ANASTOMOSIS ULCER

AE Stopped Rx Day	85 (28 DAYS AFTER LAST TREATMENT)
Duration of AE	73 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INCREASED ACTIVITY OF CROHN'S DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

日本の治験責任医師からの報告。本被験者は3[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，クローン病悪化の事象を発現した。

Event 1 の臨床経過：

投与 13 日後，被験者はクローン病悪化を発現した。投与 85 日後，クローン病悪化は消失した。

投与 22 日後，クローン病悪化のため，被験者はソル・メドロールによるステロイドパルス療法を開始した。結果として症状は改善しなかったため，投与 28 日後，被験者は入院した。被験者は消化管安静となり，精密検査を受けた。画像診断が行われ，吻合部潰瘍が認められた。投与 36 日後，被験者の症状は改善した。投与 38 日後，被験者は退院した。

投与された薬剤は，ソル・メドロールであった。

The patient’s past medications include:

GASTER D TABLETS for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

ECABET NA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

TALION TABLETS for POMPHOLXY ECZEMA ([redacted] 20[redacted] - [redacted] 20[redacted])

STELARA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PENTASA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Crohn's disease aggravated (10011403) (Crohn's disease (10011401)) [v.23.0] [10011403]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of WORSENING OF CROHN'S DISEASE

- Investigator: INCREASED ACTIVITY OF CROHN'S DISEASE

- AbbVie: event is more likely related to pre-existing crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Anastomosis ulcer sigmoid colon wall thickening.

[redacted] **20[redacted] COLONOSCOPY:** Anastomosis ulcer.

[redacted] **20[redacted] CRP:** 0.48 mg/dL (normal 0 to 0.14)

[redacted] **20[redacted] CRP:** 0.93 mg/dL (normal 0 to 0.14)

[redacted] **20[redacted] CRP:** 0.59 mg/dL (normal 0 to 0.14)

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
クローン病	X	X		
下痢		X		
発熱		X		
嘔吐		X		

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	4[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: ANAL ABSCESS	20[redacted]
CROHN'S DISEASE	20[redacted]
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
OTHER: PLATELET INCREASE DISEASE	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF PERINEAL ABSCESS	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CIGARETTES	FORMER	10 CIGARETTE	9	20[redacted]
CHEWING TOBACCO	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BCG Vaccine	Not reported.	Not reported.	Y-M: 20[redacted] / -324

MESALAZINE	Not reported.	Not reported.	Y-M: 20[redacted] / -295
ADALIMUMAB	160 mg	Not reported.	Y-M: 20[redacted] / -267
ADALIMUMAB	80 mg	Not reported.	Y-M: 20[redacted] / -253
ADALIMUMAB	40 mg	Not reported.	Y-M: 20[redacted] / -239
ADALIMUMAB	80 mg	Not reported.	Y-M: 20[redacted] / -169
INFLIXIMAB	250 mg	Not reported.	Y-M: 20[redacted] / -127
IRON	50 mg	QD	Y-M: 20[redacted] / -113
AMINO ACIDS NOS W/CARBOHYDRATES NOS	Not reported.	Not reported.	Y-M: 20[redacted] / -51
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / -51
MOVIPREP	1 L	QD	Y-M: 20[redacted] / -24
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -24
FLUMAZENIL	0.5 mg	QD	Y-M: 20[redacted] / -23
MIDAZOLAM	10 ug	QD	Y-M: 20[redacted] / -23
PENTAZOCINE	15 mg	QD	Y-M: 20[redacted] / -23

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
BCG Vaccine	Not reported.	Not reported.	Y-M: 20[redacted] / -324	Not reported.
MESALAZINE	Not reported.	Not reported.	Y-M: 20[redacted] / -295	ONGOING
IRON	50 mg	QD	Y-M: 20[redacted] / -113	ONGOING
AMINO ACIDS NOS W/CARBOHYDRATES NOS	Not reported.	Not reported.	Y-M: 20[redacted] / -51	ONGOING
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / -51	ONGOING
MOVIPREP	1 L	QD	Y-M: 20[redacted] / -24	Y-M: 20[redacted] / -24
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -24	Y-M: 20[redacted] / -24
FLUMAZENIL	0.5 mg	QD	Y-M: 20[redacted] / -23	Y-M: 20[redacted] / -23
MIDAZOLAM	10 ug	QD	Y-M: 20[redacted] / -23	Y-M: 20[redacted] / -23
PENTAZOCINE	15 mg	QD	Y-M: 20[redacted] / -23	Y-M: 20[redacted] / -23
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / 2	ONGOING
IRON	80 mg	QD	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 37
CEFMETAZOLE	1 g	BID	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
VANCOMYCIN	1 g	BID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 36

RED BLOOD CELLS	2 IU	QD	Y-M: 20[redacted]-[redacted] / 30	Y-M: 20[redacted]-[redacted] / 30
RED BLOOD CELLS	2 IU	QD	Y-M: 20[redacted]-[redacted] / 31	Y-M: 20[redacted]-[redacted] / 31

Event #1: AE Leading to Discontinuation of Study Drug

Event Description	DIARRHEA
Preferred term	下痢
AE Onset Date / Rx Day	[redacted]20[redacted] / 2 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
Not Applicable	
Microbiology	
Not Applicable	
SAE Supplemental Procedure	
Not Applicable	
AE Stopped Rx Day	36 (35 DAYS AFTER LAST TREATMENT)
Duration of AE	35 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	Not Applicable
Discontinued Study Drug Due to the Event	YES
SAE Criteria	None

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	FEVER
Preferred term	発熱
AE Onset Date / Rx Day	[redacted]20[redacted] / 2 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
Not Applicable	
Microbiology	
Not Applicable	
SAE Supplemental Procedure	
Not Applicable	
AE Stopped Rx Day	6 (5 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	Not Applicable
Discontinued Study Drug Due to the Event	YES
SAE Criteria	None

Event #3: AE Leading to Discontinuation of Study Drug

Event Description	VOMITING
Preferred term	嘔吐
AE Onset Date / Rx Day	[redacted]20[redacted] / 2 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
Not Applicable	
Microbiology	
Not Applicable	
SAE Supplemental Procedure	
Not Applicable	
AE Stopped Rx Day	23 (22 DAYS AFTER LAST TREATMENT)
Duration of AE	22 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	Not Applicable
Discontinued Study Drug Due to the Event	YES
SAE Criteria	None

Event #4: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	CROHN'S DISEASE AGGRAVATED
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 22 (21 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
[redacted]20[redacted] (Rx Day 29): Hemoglobin: 6.7 [13.7 - 16.8] g/dL; [redacted]20[redacted] (Rx Day 31): Hemoglobin: 7.1 [13.7 - 16.8] g/dL; [redacted]20[redacted] (Rx Day 33): Hemoglobin: 8.4 [13.7 - 16.8] g/dL	
Microbiology	
Not reported	
SAE Supplemental Procedure	
Not reported	
AE Stopped Rx Day	37 (36 DAYS AFTER LAST TREATMENT)
Duration of AE	16 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INADEQUATE RESPONSE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

日本の治験責任医師からの報告。本被験者は 4[redacted] 歳男性であり，AbbVie の ABBV-066（リサンキズマブ）の治験で盲検化された治験薬が投与され，クローン病増悪の事象を発現した。

Event 4 の臨床経過：

関連する病歴は，元喫煙者（1 日 10 本を 9 年間），肛門膿瘍，会陰膿瘍のドレナージ，クローン病（A2，L3：回腸・結腸，B2：狭窄型）及び鉄欠乏性貧血であった。

投与 22 日後，被験者はクローン病増悪を発現した。投与 37 日後，クローン病増悪は消失した。

投与 22 日後，被験者は Week 4 の規定来院のため治験実施施設を受診した。被験者は下痢及び嘔吐（非重篤な有害事象）を訴えた。同日，この被験者の治験は中止され，被験者は原疾患であるクローン病の悪化のため入院した。投与 24 日後，被験者はウステキヌマブ 260 mg の投与を受けた。投与 26 日後の入院中，被験者は末梢静脈カテーテル血流感染（非重篤な有害事象）を発現した。投与 30 日後，被験者のヘモグロビンは 6.7 であり，赤血球輸血が行われた。徐々に食事が再開された。投与 31 日後，被験者のヘモグロビンは 7.1 であり，赤血球輸血が行われた。投与 36 日後，下痢（非重篤な有害事象）は消失した。投与 37 日後，末梢静脈カテーテル血流感染（非重篤な有害事象）は消失した。同日，被験者の状態が良好であると判断され，被験者は退院した。

投与された薬剤は，赤血球製剤（白血球除去済み），セフメタゾール，バンコマイシン塩酸塩及びフェジンであった。

The patient’s past medications include:

PENTASA for CROHN'S DIS (Started [redacted] 20[redacted])

ADALIMUMAB for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

ELENTAL for CROHN'S DISEASE (Started [redacted] 20[redacted])

Causality for ABBV-066 (Blinded)

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1) Crohn's disease aggravated (10011403) (Crohn's disease (10011401)) [v.23.1] [10011403]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABBV-066 (Blinded)

Event of CROHN'S DISEASE AGGRAVATED

- Investigator: INADEQUATE RESPONSE

- AbbVie: EVENT MORE LIKELY RELATED TO PRE-EXISTING CROHN'S DISEASE

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] HEMOGLOBIN:** 6.7 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] HEMOGLOBIN:** 7.1 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] HEMOGLOBIN:** 8.4 G/DL (normal 13.7 to 16.8)

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
クローン病	X	X		

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	3[redacted]	FEMALE	ASIAN

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): BIOPSY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BCG Vaccine	Not reported.	Not reported.	Y-M: 19[redacted]
INFLIXIMAB	270 mg	OTHER: WEEK0,WEEK2,WEEK6	Y-M: 20[redacted]
INFLIXIMAB	270 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
AZATHIOPRINE	75 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	75 mg	QD	Y-M: 20[redacted]

HYDROCORTISONE	ADEQUATE DOSE OTHER: ADEQUATE DOSE	BID	Y-M: 20[redacted] / -288
BIO-THREE	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -274
CLOSTRIDIUM BUTYRICUM	2 g	TID	Y-M: 20[redacted] / -274
MESALAZINE	2000 mg	BID	Y-M: 20[redacted] / -274
OSMOSAL	500 mL	QD	Y-M: 20[redacted] / -87
BETAMETHASONE	ADEQUATE DOSE OTHER: ADEQUATE DOSE	QD	Y-M: 20[redacted] / -57
ALGINIC ACID	10 mL	QD	Y-M: 20[redacted] / -39
FLUMAZENIL	0.25 mg	QD	Y-M: 20[redacted] / -39
HYOSCINE	10 mg	QD	Y-M: 20[redacted] / -39
LIDOCAINE	ADEQUATE DOSE OTHER: ADEQUATE DOSE	PRN	Y-M: 20[redacted] / -39
MAALOX	10 mL	QD	Y-M: 20[redacted] / -39
MIDAZOLAM	6 mg	QD	Y-M: 20[redacted] / -39
MOVIPREP	1 OTHER: BAG	QD	Y-M: 20[redacted] / -39
NALOXONE	0.2 mg	QD	Y-M: 20[redacted] / -39
PETHIDINE	35 mg	QD	Y-M: 20[redacted] / -39

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
BCG Vaccine	Not reported.	Not reported.	Y-M: 19[redacted]	Not reported.
HYDROCORTISONE	ADEQUATE DOSE OTHER: ADEQUATE DOSE	BID	Y-M: 20[redacted] / -288	ONGOING
BIO-THREE	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -274	ONGOING
CLOSTRIDIUM BUTYRICUM	2 g	TID	Y-M: 20[redacted] / -274	ONGOING
MESALAZINE	2000 mg	BID	Y-M: 20[redacted] / -274	ONGOING
CINAL	1 g	BID	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 52
IRON	50 mg	BID	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 52
VALACICLOVIR	500 mg	BID	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 29
PARACETAMOL	200 mg	PRN	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 34
CEFCAPENE	100 mg	TID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 34

TRANEXAMIC ACID	250 mg	TID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 34
AMINO ACIDS NOS W/CARBOHYDRATES NOS	80 g	BID	Y-M: 20[redacted] / 36	ONGOING
VITAMEDIN	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 36
OSMOSAL	500 mL	QD	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 53
VITAMEDIN	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 53
CINAL	2 g	BID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 64
ECABET	1.5 g	BID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 64
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 64
IRON	100 mg	BID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 64
CEFAZOLIN	2 g	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 58
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 58
IRON	80 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 58
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 58
VEEN D	500 mL	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 58
VITAMEDIN	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 58
PARACETAMOL	200 mg	PRN	Y-M: 20[redacted] / 59	ONGOING
CEFAZOLIN	2 g	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
IRON	80 mg	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
VEEN D	500 mL	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
VITAMEDIN	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
CEFAZOLIN	2 g	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 64
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 80

IRON	80 mg	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 80
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 80
VEEN D	500 mL	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 80
VITAMEDIN	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 80
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 79
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / 66	ONGOING
FOSFOMYCIN	1 g	TID	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 71
CINAL	1 g	BID	Y-M: 20[redacted] / 69	ONGOING
IRON	50 mg	BID	Y-M: 20[redacted] / 69	ONGOING
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 69
PENTAZOCINE	15 mg	QD	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 69
MICAFUNGIN	150 mg	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 80
INFLIXIMAB	300 mg	OTHER: WEEK0,WEEK2, WEEK6	Y-M: 20[redacted] / 74	ONGOING
DEXCHLORPHENIRAMINE	5 mg	QD	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 74
HYDROCORTISONE	300 mg	QD	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 74

Event #1: AE Leading to Discontinuation of Study Drug

Event Description	EXACERBATION OF CROHN'S DISEASE
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 15
Age at AE Onset	3[redacted]
Laboratory Testing	
Not Applicable	
Microbiology	
Not Applicable	
SAE Supplemental Procedure	
Not Applicable	
AE Stopped Rx Day	64 (11 DAYS AFTER LAST TREATMENT)
Duration of AE	50 DAYS
Severity	Moderate

Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	Not Applicable
Discontinued Study Drug Due to the Event	YES
SAE Criteria	None

Event #2: Serious Adverse Event

Event Description	EXACERBATION OF CROHN'S DISEASE
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 65 (12 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 65): Albumin: 2.4 [4 - 5] g/dL; C Reactive Protein: 22.2 [0 - 2.8] mg/L; Hemoglobin: 9.7 [11 - 15] g/dL; NPTST091-ESR: 81 [2 - 15] mm/h; Platelets: 575 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 67): Albumin: 2.3 [4 - 5] g/dL; C Reactive Protein: 20.1 [0 - 2.8] mg/L; Hemoglobin: 9.5 [11 - 15] g/dL; NPTST091-ESR: 71 [2 - 15] mm/h; Platelets: 570 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 69): Albumin: 2.4 [4 - 5] g/dL; C Reactive Protein: 21.1 [0 - 2.8] mg/L; Hemoglobin: 10.2 [11 - 15] g/dL; NPTST091-ESR: 70 [2 - 15] mm/h; Platelets: 522 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 70): Albumin: 2.4 [4 - 5] g/dL; C Reactive Protein: 15.9 [0 - 2.8] mg/L; Hemoglobin: 10.4 [11 - 15] g/dL; NPTST091-ESR: 75 [2 - 15] mm/h; Platelets: 498 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 71): Albumin: 2.2 [4 - 5] g/dL; C Reactive Protein: 14.3 [0 - 2.8] mg/L; Hemoglobin: 8.9 [11 - 15] g/dL; NPTST091-ESR: 67 [2 - 15] mm/h; Platelets: 489 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 72): Albumin: 2.2 [4 - 5] g/dL; Hemoglobin: 9.4 [11 - 15] g/dL; Platelets: 464 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 73): Albumin: 2.4 [4 - 5] g/dL; C Reactive Protein: 11.3 [0 - 2.8] mg/L; Hemoglobin: 9.6 [11 - 15] g/dL; NPTST091-ESR: 67 [2 - 15] mm/h; Platelets: 454 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 74): C Reactive Protein: 16.6 [0 - 2.8] mg/L; Hemoglobin: 10.7 [11 - 15] g/dL; NPTST091-ESR: 77 [2 - 15] mm/h; Platelets: 484 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 75): Albumin: 2.4 [4 - 5] g/dL; C Reactive Protein: 11.3 [0 - 2.8] mg/L; Hemoglobin: 9.6 [11 - 15] g/dL; NPTST091-ESR: 64 [2 - 15] mm/h; Platelets: 442 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 76): Hemoglobin: 10.1 [11 - 15] g/dL; Platelets: 440 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 77): Albumin: 2.5 [4 - 5] g/dL; C Reactive Protein: 4.9 [0 - 2.8] mg/L; Hemoglobin: 9.8 [11 - 15] g/dL; NPTST091-ESR: 66 [2 - 15] mm/h; Platelets: 464 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 79): Albumin: 2.6 [4 - 5] g/dL; C Reactive Protein: 3.8 [0 - 2.8] mg/L; Hemoglobin: 9.9 [11 - 15] g/dL; NPTST091-ESR: 49 [2 - 15] mm/h; Platelets: 461 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 81): Albumin: 2.9 [4 - 5] g/dL; C Reactive Protein: 35.8 [0 - 2.8] mg/L; Hemoglobin: 10.3 [11 - 15] g/dL; NPTST091-ESR: 78 [2 - 15] mm/h; Platelets: 507 [120 - 356] 10^3/uL; [redacted]20[redacted] (Rx Day 84): Albumin: 3.0 [4 - 5] g/dL; C Reactive Protein: 24.7 [0 - 2.8] mg/L; Hemoglobin: 10.6 [11 - 15] g/dL; NPTST091-ESR: 76 [2 - 15] mm/h; Platelets: 534 [120 - 356] 10^3/uL

Microbiology

Not reported

SAE Supplemental Procedure

Not reported

AE Stopped Rx Day	86 (33 DAYS AFTER LAST TREATMENT)
Duration of AE	22 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	THE EVENT CAN BE ATTRIBUTED TO THE PRIMARY DISEASE PROGRESSION.
Discontinued Study Drug Due to the Event	NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted] 20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

日本の治験責任医師からの報告。本被験者は 3[redacted] 歳女性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，クローン病増悪の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，クローン病，非喫煙者及び飲酒者（1 日 2 杯未満）であった。

投与 65 日後，被験者はクローン病増悪を発現した。投与 86 日後，クローン病増悪は消失した。

投与 15 日後から投与 64 日後まで，被験者は非重篤なクローン病増悪を発現した。本事象により治験薬の投与は完全に中止された。

投与 65 日後，被験者は心窩部痛増悪，栄養障害及び鉄欠乏性貧血のため入院した。被験者は病院で治療を受け，臨床検査を受けた。投与 86 日後，被験者は上腹部痛及び下痢を発現しておらず，全身状態が改善していたため，退院した。

投与された薬剤は，アタラックス-P，ミカファンギンナトリウム，レミケード，ソセゴン，ホスホマイシンナトリウム，ビーフリード及びゼンタコートであった。

The patient's past medications include:

REMICADE for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

IMURAN for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

AZANIN for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

RINDERON for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Crohn's disease aggravated (10011403) (Crohn's disease (10011401)) [v.23.1] [10011403]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of EXACERBATION OF CROHN'S DISEASE

- Investigator: The event can be attributed to the primary disease progression.

- AbbVie: Event more likely related to pre-existing Crohn's Disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 2.4 G/DL (normal 4 to 5)

[redacted] **20[redacted] ALBUMIN:** 2.2 G/DL (normal 4 to 5)

[redacted] **20[redacted] ALBUMIN:** 3.0 G/DL (normal 4 to 5)

[redacted] **20[redacted] ESR:** 81 mm/h (normal 2 to 15)

[redacted] **20[redacted] ESR:** 67 mm/h (normal 2 to 15)

[redacted] **20[redacted] ESR:** 49 mm/h (normal 2 to 15)

[redacted] **20[redacted] ESR:** 76 mm/h (normal 2 to 15)

[redacted] **20[redacted] HEMOGLOBIN:** 9.7 G/DL (normal 11 to 15)

[redacted] **20[redacted] HEMOGLOBIN:** 8.9 G/DL (normal 11 to 15)

[redacted] **20[redacted] HEMOGLOBIN:** 9.6 G/DL (normal 11 to 15)

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

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 22.2 MG/L (normal 0 to 2.8)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 11.3 MG/L (normal 0 to 2.8)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 3.8 MG/L (normal 0 to 2.8)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 24.7 MG/L (normal 0 to 2.8)

[redacted] **20[redacted] PLATELET COUNT:** 575 X10**3/uL (normal 120 to 356)

[redacted] **20[redacted] PLATELET COUNT:** 454 X10**3/uL (normal 120 to 356)

[redacted] **20[redacted] PLATELET COUNT:** 534 X10**3/uL (normal 120 to 356)

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
亜イレウス	X			

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO / P2:RZB 1200 MG IV	2[redacted]	MALE	ASIAN

Medical History	Onset Year
PANCREATITIS: DRUG-INDUCED PANCREATITIS	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: LYMPHOCYTE COUNT DECREASED	20[redacted]
PANCREATITIS: DRUG-INDUCED PANCREATITIS	20[redacted]
OTHER: PERIANAL ABSCESS	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
Risankizumab	1200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 80	[redacted]20[redacted] / 134	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BCG Vaccine	Not reported.	Not reported.	Y-M: 19[redacted]
MESALAZINE	4000 mg	QD	Y-M: 20[redacted]

AMINO ACIDS NOS W/CARBOHYDRATES NOS	80 g	BID	Y-M: 20[redacted]
AZATHIOPRINE	25 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
CLOSTRIDIUM BUTYRICUM	1 OTHER: TABLET	TID	Y-M: 20[redacted]
MERCAPTOPURINE	35 mg	QD	Y-M: 20[redacted]
MESALAZINE	4000 mg	QD	Y-M: 20[redacted]
MERCAPTOPURINE	40 mg	QD	Y-M: 20[redacted] / -248
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -84

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
BCG Vaccine	Not reported.	Not reported.	Y-M: 19[redacted]	Not reported.
CLOSTRIDIUM BUTYRICUM	1 OTHER: TABLET	TID	Y-M: 20[redacted]	ONGOING
AMINO ACIDS NOS W/CARBOHYDRATES NOS	80 g	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 104
MERCAPTOPURINE	40 mg	QD	Y-M: 20[redacted] / -248	Y-M: 20[redacted] / 142
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 81
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 87
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	QD	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 105
SOLACET F	500 mL	QD	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 105
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 109
HYOSCINE	20 mg	PRN	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 111
VITAMEDIN	1 OTHER: VIAL	QD	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 113
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	BID	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 109
VEEN D	500 mL	BID	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 109
PENTAZOCINE	7.5 mg	PRN	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 114
MIDAZOLAM	AS NEEDED mg	PRN	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 123
PENTAZOCINE	15 mg	PRN	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 123

HYDROXYZINE	12.5 mg	PRN	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 149
CEFMETAZOLE	1 g	BID	Y-M: 20[redacted] / 107	Y-M: 20[redacted] / 111
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 113
VEEN D	500 mL	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 113
AMINO ACIDS NOS W/CARBOHYDRATES NOS	1 OTHER: PACK	PRN	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 124
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 121
CARBAZOCHROME	100 mg	QD	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	QD	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
TRANEXAMIC ACID	1000 mg	QD	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
MAGNESIUM OXIDE	330 mg	TID	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 122
CARBAZOCHROME	100 mg	BID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 117
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 117
TRANEXAMIC ACID	1000 mg	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 117
VEEN D	500 mL	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 117
VEEN D	500 mL	QD	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 120
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	BID	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 125
TRANEXAMIC ACID	1000 mg	QD	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 125
VEEN D	500 mL	BID	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 121
CARBAZOCHROME	100 mg	BID	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 125
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	QD	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 125
VEEN D	500 mL	QD	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 125

MAGNESIUM OXIDE	330 mg	TID	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 146
AMINO ACIDS NOS W/CARBOHYDRATES NOS	1 OTHER: PACK	PRN	Y-M: 20[redacted] / 129	Y-M: 20[redacted] / 146
VEEN D	500 mL	QD	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 147
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	BID	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 148
ATROPINE	0.5 mg	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
CEFMETAZOLE	1 g	TID	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
FENTANYL	10 mL	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
FLURBIPROFEN	50 mg	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
PHYSIO 140	500 mL	BID	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
PROPOFOL	140 mg	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
REMIFENTANIL	0.6 mg	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
ROCURONIUM	120 mg	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
ROPIVACAINE	13.47 mL	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
ROPIVACAINE	4 mL	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
ROPIVACAINE	8 mL	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
SOLACET F	500 mL	TID	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
VEEN D	500 mL	BID	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 149
FAMOTIDINE	10 mg	PRN	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 151
KETOPROFEN	40 mg	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 154
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 155
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	BID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
CEFMETAZOLE	1 g	QD	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149

AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	TID	Y-M: 20[redacted] / 150	Y-M: 20[redacted] / 151
VEEN D	500 mL	QD	Y-M: 20[redacted] / 150	Y-M: 20[redacted] / 153
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	BID	Y-M: 20[redacted] / 152	Y-M: 20[redacted] / 152
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	TID	Y-M: 20[redacted] / 153	Y-M: 20[redacted] / 153
AMINO ACIDS NOS W/CARBOHYDRATES NOS	1 OTHER: PACK	PRN	Y-M: 20[redacted] / 153	Y-M: 20[redacted] / 155
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	BID	Y-M: 20[redacted] / 154	Y-M: 20[redacted] / 155
VEEN D	500 mL	QD	Y-M: 20[redacted] / 155	Y-M: 20[redacted] / 156
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL	QD	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 156
AMINO ACIDS NOS W/COPPER/ELECTROLYTES NOS/GLU	1000 mL	BID	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 157
GLYCINE MAX	100 mL	QD	Y-M: 20[redacted] / 157	ONGOING
AMINO ACIDS NOS W/COPPER/ELECTROLYTES NOS/GLU	1000 mL	BID	Y-M: 20[redacted] / 158	ONGOING
AMINO ACIDS NOS W/CARBOHYDRATES NOS	1 OTHER: PACK	PRN	Y-M: 20[redacted] / 170	ONGOING

Event #1: Serious Adverse Event

Event Description	SUBILEUS
Preferred term	亜イレウス
AE Onset Date / Rx Day	[redacted]20[redacted] / 104
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 127): Leukocytes: 2.65 [3.3 - 8.8] 10^3/uL

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 105): CT: SUBILEUS; CT SCAN: SUBILEUS; ENDOSCOPIC DILATION: SUBILEUS; ENDOSCOPY: SUBILEUS; ENDOSCOPY: SUBILEUS; ENDOSCOPY: SUBILEUS; ENDOSCOPY: SUBILEUS; ENDOSCOPY: SUBILEUS; ILEUS TUBE INSERTION: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; [redacted]20[redacted] (Rx Day 135): CT SCAN: SUBILEUS; CT SCAN: SUBILEUS; PARTIAL

COLECTOMY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; X-RAY: SUBILEUS; [redacted]20[redacted] (Rx Day 166): X-RAY: SUBILEUS

AE Stopped Rx Day	183 (49 DAYS AFTER LAST TREATMENT)
Duration of AE	80 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN'S DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

日本の治験責任医師からの報告。本被験者は2[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，亜イレウスの事象を発現した。

Event 1 の臨床経過：

関連する病歴は，薬剤誘発性膵炎，クローン病，リンパ球数減少，肛門周囲膿瘍，非喫煙者及び非飲酒者であった。

投与 104 日後，被験者は亜イレウスを発現した。投与 183 日後，亜イレウスは消失した。

投与 104 日後，被験者は食欲減退及び腹痛増加を発現した。投与 105 日後，X 線及び CT 検査の結果，亜イレウスが認められた。同日，被験者は腹痛及び嘔吐のため入院した。被験者には便の減少も認められた。投与 106 日後，イレウスに対して内視鏡的拡張術及びイレウス管挿入が行われた。投与 113 日後，イレウスに対して内視鏡的拡張術が行われ，イレウス管は抜去された。投与 116 日後，X 線で亜イレウスの再発が認められた。内視鏡的拡張術が行われた。投与 121 日後，X 線で亜イレウスの再発が認められた。内視鏡的拡張術が行われた。投与 123 日後，イレウス管挿入が行われた。投与 148 日後，イレウスに対して外科的腸切除が行われた。投与 169 日後，被験者は M16-000 試験にロールオーバーされ，治験薬が投与された。投与 183 日後，経過が良好であったため被験者は退院した。

投与された薬剤は，ソリューゲン F，ヴィーン D，ビーフリード，イントラリポス輸液 20%，ブスコパン，ビタメジン静注用，ソセゴン，アタラックス-P，セフメタゾン，レボフロキサシン，ソルデム 3A，カルバゾクロムスルホン酸ナトリウム，トラネキサム酸，マグミット，ガスター，エルネオパ NF2 号及びメトクロプラミドであった。

The patient’s past medications include:

PENTASA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

AZANIN for CROHN'S DIEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

ZENTACORT for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

LEVOFLOXACIN for ENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Subileus (10050396) (Subileus (10050396)) [v.23.1] [10050396]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of SUBILEUS

- Investigator: Crohn's Disease

- AbbVie: Event more likely related to underlying Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL CT: subileus

[redacted] 20[redacted] CT SCAN: Subileus.

[redacted] 20[redacted] ENDOSCOPY: Subileus.

[redacted] **20[redacted] WBC:** 2.65 X10**3/MCL (normal 3.3 to 8.8)

[redacted] 20[redacted] X-RAY: subileus

[redacted] **20[redacted] X-RAY:** recurrence of subileus

[redacted] 20[redacted] X-RAY: Subileus.

[redacted] **20[redacted] X-RAY:** recurrence of subileus

[redacted] 20[redacted] X-RAY: Subileus.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
胆管結石	X			
胆管炎	X			
急性胆嚢炎	X			

Treatment Group	Age at Study Start	Sex	Race
P1:RZB 600 MG IV / P2:RZB 1200 MG IV	4[redacted]	MALE	ASIAN

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
DEPRESSION: DEPRESSION	20[redacted]
OTHER: HEADACHE	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: GERD	20[redacted]
OTHER: VENUS THROMBOSIS	20[redacted]
PERIPHERAL NERVE DISORDER: PERIPHERAL NEUTOPATHY	20[redacted]
HYPERLIPIDEMIA: HYPERLIPIDEMIA	20[redacted]
OTHER: IBS	20[redacted]
CHOLELITHIASIS	20[redacted]
OTHER: BRONCHITIS	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CIGARETTES	FORMER	15 CIGARETTE	8	20[redacted]
CHEWING TOBACCO	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	2 - 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted] / 1	[redacted] / 55	55
Risankizumab	1200 mg	IV	Every 4 Weeks	[redacted] / 91	[redacted] / 148	58

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
INFLIXIMAB	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: [redacted]
VALPROIC ACID	200 mg	BID	Y-M: [redacted]
AZATHIOPRINE	50 mg	QD	Y-M: [redacted]
ADALIMUMAB	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: [redacted]
ESOMEPRAZOLE	20 mg	QD	Y-M: [redacted]
IRON	100 mg	QD	Y-M: [redacted]
EDOXABAN	30 mg	QD	Y-M: [redacted]
MESALAZINE	1000 mg	TID	Y-M: [redacted]
AMITRIPTYLINE	10 mg	BID	Y-M: [redacted]
AMITRIPTYLINE	25 mg	QD	Y-M: [redacted]
MIRTAZAPINE	30 mg	QD	Y-M: [redacted]
SULPIRIDE	50 mg	BID	Y-M: [redacted]
SUVOREXANT	15 mg	QD	Y-M: [redacted]
TRAMADOL	75 mg	QID	Y-M: [redacted]
ADALIMUMAB	UNKNOWN OTHER: UNKNOWN	OTHER: EVERY 2 WEEKS	Y-M: [redacted]
AZATHIOPRINE	50 mg	QD	Y-M: [redacted]
COLESTILAN	1500 mg	BID	Y-M: [redacted]
RAMOSETRON	10 ug	QD	Y-M: [redacted]
CINAL	200 mg	TID	Y-M: [redacted]
USTEKINUMAB	90 mg	OTHER: EVERY 8 WEEKS	Y-M: [redacted]
PARACETAMOL	400 mg	PRN	Y-M: [redacted] / -284
AMBROXOL	45 mg	PRN	Y-M: [redacted] / -240
MEXILETINE	100 mg	TID	Y-M: [redacted] / -240
ALBUMIN TANNATE	1 g	TID	Y-M: [redacted] / -203
FLAVINE ADENINE DINUCLEOTIDE	10 mg	TID	Y-M: [redacted] / -203
PREGABALIN	75 mg	QD	Y-M: [redacted] / -203
AMINO ACIDS NOS W/CARBOHYDRATES NOS	240 g	QD	Y-M: [redacted] / -147
LOPERAMIDE	2 mg	BID	Y-M: [redacted] / -141
SENNOSIDE A+B	48 mg	QD	Y-M: [redacted] / -8
MOVIPREP	1800 mL	QD	Y-M: [redacted] / -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
VALPROIC ACID	200 mg	BID	Y-M: 20[redacted]	ONGOING
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]	ONGOING
IRON	100 mg	QD	Y-M: 20[redacted]	ONGOING
EDOXABAN	30 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 71
MESALAZINE	1000 mg	TID	Y-M: 20[redacted]	ONGOING
AMITRIPTYLINE	10 mg	BID	Y-M: 20[redacted]	ONGOING
AMITRIPTYLINE	25 mg	QD	Y-M: 20[redacted]	ONGOING
MIRTAZAPINE	30 mg	QD	Y-M: 20[redacted]	ONGOING
TRAMADOL	75 mg	QID	Y-M: 20[redacted]	ONGOING
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]	ONGOING
COLESTILAN	1500 mg	BID	Y-M: 20[redacted]	ONGOING
RAMOSETRON	10 ug	QD	Y-M: 20[redacted]	ONGOING
CINAL	200 mg	TID	Y-M: 20[redacted]	ONGOING
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / -284	ONGOING
AMBROXOL	45 mg	PRN	Y-M: 20[redacted] / -240	ONGOING
MEXILETINE	100 mg	TID	Y-M: 20[redacted] / -240	ONGOING
ALBUMIN TANNATE	1 g	TID	Y-M: 20[redacted] / -203	ONGOING
FLAVINE ADENINE DINUCLEOTIDE	10 mg	TID	Y-M: 20[redacted] / -203	ONGOING
AMINO ACIDS NOS W/CARBOHYDRATES NOS	240 g	QD	Y-M: 20[redacted] / -147	Y-M: 20[redacted] / 64
LOPERAMIDE	2 mg	BID	Y-M: 20[redacted] / -141	ONGOING
PREGABALIN	50 mg	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 79
ELETRIPTAN	20 mg	PRN	Y-M: 20[redacted] / 9	ONGOING
CHLORPROMAZINE	12.5 mg	BID	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 65
SUVOREXANT	10 mg	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 110
ACETYLCYSTEINE W/ALANINE/ARGININE/ASCORBIC AC	1000 mL	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 69
CEFOTAXIME	1 g	BID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 75
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	QD	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 69

CHLORPROMAZINE	12.5 mg	BID	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 83
FLUMAZENIL	0.5 mg	QD	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
MIDAZOLAM	10 mg	QD	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
NAFAMOSTAT	50 mg	QD	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
PETHIDINE	35 mg	QD	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
ULINASTATIN	50000 OTHER: UNIT	QD	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 68
AMINO ACIDS NOS W/CARBOHYDRATES NOS	240 g	QD	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 70
PARACETAMOL	1000 mg	BID	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 71
ACETYLCYSTEINE W/ALANINE/ARGININE/ASCORBIC AC	1000 mL	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 75
DEXTROSE IN LACTATED RINGER'S	500 mL	QD	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 72
VITAMEDIN	100 mg	QD	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 72
DEXTROSE IN LACTATED RINGER'S	500 mL	QD	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 75
VITAMEDIN	100 mg	QD	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 75
AMINO ACIDS NOS W/CARBOHYDRATES NOS	80 g	QD	Y-M: 20[redacted] / 75	Y-M: 20[redacted] / 75
AMINO ACIDS NOS W/CARBOHYDRATES NOS	160 g	QD	Y-M: 20[redacted] / 76	Y-M: 20[redacted] / 76
EDOXABAN	30 mg	QD	Y-M: 20[redacted] / 76	Y-M: 20[redacted] / 107
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 77
SENNOSIDE A+B	48 mg	QD	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 77
AMINO ACIDS NOS W/CARBOHYDRATES NOS	240 g	QD	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 108
COLYTE	2500 mL	QD	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 78

DIAZEPAM	10 mg	QD	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 78
PREGABALIN	75 mg	QD	Y-M: 20[redacted] / 80	ONGOING
CHLORPROMAZINE	12.5 mg	BID	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 109
DEXTROSE IN LACTATED RINGER'S	500 mL	QD	Y-M: 20[redacted] / 94	Y-M: 20[redacted] / 94
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 94	Y-M: 20[redacted] / 94
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 94	Y-M: 20[redacted] / 120
REBAMIPIDE	100 mg	PRN	Y-M: 20[redacted] / 94	Y-M: 20[redacted] / 120
ACETYLCYSTEINE W/ALANINE/ARGININE/ASCORBIC AC	1000 mL	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 109
CEFOTAXIME	1 g	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 109
DEXTROSE IN LACTATED RINGER'S	500 mL	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 109
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 109
PENTAZOCINE	15 mg	PRN	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 110
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	TID	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 110
DICLOFENAC	25 mg	PRN	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 110
ENOXAPARIN	2000 IU	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 110
HYOSCINE	20 mg	PRN	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 110
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 110
FENTANYL	0.3 mg	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 112
CEFOTAXIME	1 g	BID	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 113
ROPIVACAINE	6 mL	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 113
ENOXAPARIN	2000 IU	BID	Y-M: 20[redacted] / 111	Y-M: 20[redacted] / 111
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	QID	Y-M: 20[redacted] / 111	Y-M: 20[redacted] / 113

PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted]-[redacted] / 111	Y-M: 20[redacted]-[redacted] / 115
FLURBIPROFEN	50 mg	PRN	Y-M: 20[redacted]-[redacted] / 111	Y-M: 20[redacted]-[redacted] / 123
CHLORPROMAZINE	12.5 mg	BID	Y-M: 20[redacted]-[redacted] / 111	Y-M: 20[redacted]-[redacted] / 151
SUVOREXANT	15 mg	QD	Y-M: 20[redacted]-[redacted] / 111	Y-M: 20[redacted]-[redacted] / 151
EDOXABAN	30 mg	QD	Y-M: 20[redacted]-[redacted] / 113	ONGOING
PARACETAMOL	400 mg	QID	Y-M: 20[redacted]-[redacted] / 113	ONGOING
DIFLUPREDNATE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]-[redacted] / 114	Y-M: 20[redacted]-[redacted] / 130
CELECOXIB	200 mg	BID	Y-M: 20[redacted]-[redacted] / 123	ONGOING

Event #1: Serious Adverse Event

Event Description	CHOLANGITIS, COMMON BILE DUCT STONE
Preferred term	胆管結石
AE Onset Date / Rx Day	[redacted]20[redacted] / 62
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 65): Alanine Aminotransferase: 144 [5 - 30] U/L; Alkaline Phosphatase: 574 [117 - 356] U/L; Aspartate Aminotransferase: 80 [11 - 30] U/L; Bilirubin: 2.3 [0.3 - 1.3] mg/dL; Leukocytes: 4600 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 73 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 11.50 [0 - 0.1] mg/dL; NPTST115-GGT: 233 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 66): Alanine Aminotransferase: 95 [5 - 30] U/L; Alkaline Phosphatase: 453 [117 - 356] U/L; Aspartate Aminotransferase: 44 [11 - 30] U/L; Bilirubin: 1.0 [0.3 - 1.3] mg/dL; Leukocytes: 3760 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 53 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 6.80 [0 - 0.1] mg/dL; NPTST115-GGT: 174 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 67): Alanine Aminotransferase: 71 [5 - 30] U/L; Alanine Aminotransferase: 56 [5 - 30] U/L; Alkaline Phosphatase: 485 [117 - 356] U/L; Alkaline Phosphatase: 470 [117 - 356] U/L; Aspartate Aminotransferase: 35 [11 - 30] U/L; Aspartate Aminotransferase: 29 [11 - 30] U/L; Bilirubin: 0.7 [0.3 - 1.3] mg/dL; Bilirubin: 0.6 [0.3 - 1.3] mg/dL; Leukocytes: 4760 [3600 - 9200] Unit not reported; Leukocytes: 3540 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 354 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 5.17 [0 - 0.1] mg/dL; NPTST050-C REACTIVE PROTEIN: 4.04 [0 - 0.1] mg/dL; NPTST115-GGT: 160 [12 - 50] U/L; NPTST115-GGT: 162 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 68): Alanine Aminotransferase: 51 [5 - 30] U/L; Alkaline Phosphatase: 497 [117 - 356] U/L; Aspartate Aminotransferase: 25 [11 - 30] U/L; Bilirubin: 0.6 [0.3 - 1.3] mg/dL; Leukocytes: 3680 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 255 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 3.14 [0 - 0.1] mg/dL; NPTST115-GGT: 160 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 71): Alanine Aminotransferase: 33 [5 - 30] U/L; Alkaline Phosphatase: 451 [117 - 356] U/L; Aspartate Aminotransferase: 26 [11 - 30] U/L; Bilirubin: 0.4 [0.3 - 1.3] mg/dL; Leukocytes: 4260 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 210 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 0.48 [0 - 0.1] mg/dL; NPTST115-GGT: 110 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 75): Alanine Aminotransferase: 37 [5 - 30] U/L; Alkaline Phosphatase: 399 [117 - 356] U/L; Aspartate Aminotransferase: 38 [11 - 30] U/L; Bilirubin: 0.6 [0.3 - 1.3] mg/dL; Leukocytes: 4870 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 113 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 0.22 [0 - 0.1] mg/dL; NPTST115-GGT: 85 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 78): Alanine Aminotransferase: 54 [5 - 30] U/L; Alkaline Phosphatase: 392 [117 - 356] U/L; Aspartate Aminotransferase: 50 [11 - 30] U/L;

Bilirubin: 0.5 [0.3 - 1.3] mg/dL; Leukocytes: 3990 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 98 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 0.09 [0 - 0.1] mg/dL; NPTST115-GGT: 69 [12 - 50] U/L

Microbiology

[redacted]20[redacted] (Rx Day 77): STOOL NPTST099-FECAL OCCULT BLOOD TEST: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 62): COLONOSCOPY: MILD INFLAMMATION WITH REDNESS AT ILEUM TERMINAL; CT: COMMON BILE STONE WAS POINTED OUT.; ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY: EST WAS PERFORMED.; ENDOSCOPIC SPHINCTEROTOMY: REMOVED A STONE IN THE BILE DUCT.; MRI: COMMON BILE DUCT STONE WAS POINTED OUT.

AE Stopped Rx Day	81
Duration of AE	20 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	GALLSTONE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	CHOLANGITIS, COMMON BILE DUCT STONE
Preferred term	胆管炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 62
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 65): Alanine Aminotransferase: 144 [5 - 30] U/L; Alkaline Phosphatase: 574 [117 - 356] U/L; Aspartate Aminotransferase: 80 [11 - 30] U/L; Bilirubin: 2.3 [0.3 - 1.3] mg/dL; Leukocytes: 4600 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 73 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 11.50 [0 - 0.1] mg/dL; NPTST115-GGT: 233 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 66): Alanine Aminotransferase: 95 [5 - 30] U/L; Alkaline Phosphatase: 453 [117 - 356] U/L; Aspartate Aminotransferase: 44 [11 - 30] U/L; Bilirubin: 1.0 [0.3 - 1.3] mg/dL; Leukocytes: 3760 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 53 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 6.80 [0 - 0.1] mg/dL; NPTST115-GGT: 174 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 67): Alanine Aminotransferase: 71 [5 - 30] U/L; Alanine Aminotransferase: 56 [5 - 30] U/L; Alkaline Phosphatase: 485 [117 - 356] U/L; Alkaline Phosphatase: 470 [117 - 356] U/L; Aspartate Aminotransferase: 35 [11 - 30] U/L; Aspartate Aminotransferase: 29 [11 - 30] U/L; Bilirubin: 0.7 [0.3 - 1.3] mg/dL; Bilirubin: 0.6 [0.3 - 1.3] mg/dL; Leukocytes: 4760 [3600 - 9200] Unit not reported; Leukocytes: 3540 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 354 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 5.17 [0 - 0.1] mg/dL; NPTST050-C REACTIVE PROTEIN: 4.04 [0 - 0.1] mg/dL; NPTST115-GGT: 160 [12 - 50] U/L; NPTST115-GGT: 162 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 68): Alanine Aminotransferase: 51 [5 - 30] U/L; Alkaline Phosphatase: 497 [117 - 356] U/L; Aspartate Aminotransferase: 25 [11 - 30] U/L; Bilirubin: 0.6 [0.3 - 1.3] mg/dL; Leukocytes: 3680 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 255 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 3.14 [0 - 0.1] mg/dL; NPTST115-GGT: 160 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 71): Alanine Aminotransferase: 33 [5 - 30] U/L; Alkaline Phosphatase: 451 [117 - 356] U/L; Aspartate Aminotransferase: 26 [11 - 30] U/L; Bilirubin: 0.4 [0.3 - 1.3] mg/dL; Leukocytes: 4260 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 210 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 0.48 [0 - 0.1] mg/dL; NPTST115-GGT: 110 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 75): Alanine Aminotransferase: 37 [5 - 30] U/L; Alkaline Phosphatase: 399 [117 - 356] U/L; Aspartate Aminotransferase: 38 [11 - 30] U/L; Bilirubin: 0.6 [0.3 - 1.3] mg/dL; Leukocytes: 4870 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 113 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 0.22 [0 - 0.1] mg/dL; NPTST115-GGT: 85 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 78): Alanine Aminotransferase:

54 [5 - 30] U/L; Alkaline Phosphatase: 392 [117 - 356] U/L; Aspartate Aminotransferase: 50 [11 - 30] U/L; Bilirubin: 0.5 [0.3 - 1.3] mg/dL; Leukocytes: 3990 [3600 - 9200] Unit not reported; NPTST012-AMYLASE: 98 [38 - 123] U/L; NPTST050-C REACTIVE PROTEIN: 0.09 [0 - 0.1] mg/dL; NPTST115-GGT: 69 [12 - 50] U/L

Microbiology

[redacted]20[redacted] (Rx Day 77): STOOL NPTST099-FECAL OCCULT BLOOD TEST: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 62): COLONOSCOPY: MILD INFLAMMATION WITH REDNESS AT ILEUM TERMINAL; CT: COMMON BILE STONE WAS POINTED OUT.; ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY: EST WAS PERFORMED.; ENDOSCOPIC SPHINCTEROTOMY: REMOVED A STONE IN THE BILE DUCT.; MRI: COMMON BILE DUCT STONE WAS POINTED OUT.

AE Stopped Rx Day	81
Duration of AE	20 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	GALLSTONE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	ACUTE CHOLECYSTITIS
Preferred term	急性胆嚢炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 109
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 109): Alanine Aminotransferase: 50 [5 - 30] U/L; Alkaline Phosphatase: 405 [117 - 356] U/L; Aspartate Aminotransferase: 36 [11 - 30] U/L; Leukocytes: 7910 [3600 - 9200] Unit not reported; NPTST050-C REACTIVE PROTEIN: 0.30 [0 - 0.1] mg/dL; NPTST115-GGT: 31 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 110): Alkaline Phosphatase: 368 [117 - 356] U/L; Aspartate Aminotransferase: 44 [5 - 30] U/L; Aspartate Aminotransferase: 30 [11 - 30] U/L; Leukocytes: 11660 [3600 - 9200] Unit not reported; NPTST050-C REACTIVE PROTEIN: 3.90 [0 - 0.1] mg/dL; NPTST115-GGT: 31 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 111): Alanine Aminotransferase: 32 [5 - 30] U/L; Alkaline Phosphatase: 251 [117 - 356] U/L; Aspartate Aminotransferase: 37 [11 - 30] U/L; Leukocytes: 8110 [3600 - 9200] Unit not reported; NPTST115-GGT: 21 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 113): Alanine Aminotransferase: 23 [5 - 30] U/L; Alkaline Phosphatase: 248 [117 - 356] U/L; Aspartate Aminotransferase: 30 [11 - 30] U/L; Leukocytes: 4810 [3600 - 9200] Unit not reported; NPTST050-C REACTIVE PROTEIN: 7.38 [0 - 0.1] mg/dL; NPTST115-GGT: 21 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 117): Alanine Aminotransferase: 33 [5 - 30] U/L; Alkaline Phosphatase: 333 [117 - 356] U/L; Aspartate Aminotransferase: 32 [11 - 30] U/L; Leukocytes: 4810 [3600 - 9200] Unit not reported; NPTST050-C REACTIVE PROTEIN: 0.81 [0 - 0.1] mg/dL; NPTST115-GGT: 30 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 120): Alanine Aminotransferase: 70 [5 - 30] U/L; Alkaline Phosphatase: 350 [117 - 356] U/L; Aspartate Aminotransferase: 49 [11 - 30] U/L; Leukocytes: 5340 [3600 - 9200] Unit not reported; NPTST050-C REACTIVE PROTEIN: 0.28 [0 - 0.1] mg/dL; NPTST115-GGT: 42 [12 - 50] U/L; [redacted]20[redacted] (Rx Day 148): Alanine Aminotransferase: 25 [5 - 30] U/L; Alkaline Phosphatase: 291 [117 - 356] U/L; Aspartate Aminotransferase: 20 [11 - 30] U/L; Leukocytes: 5060 [3600 - 9200] Unit not reported; NPTST115-GGT: 23 [12 - 50] U/L

Microbiology

Not reported

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 93): ABDOMINAL ULTRASOUND: STONE IN GALLBLADDER NECK; CHOLECYSTECTOMY: REMOVED THE GALLBLADDER BY OPEN TECHNIQUE; CT: STONE IN GALLBLADDER NECK; HISTOPATHOLOGY: ACUTE CHOLECYSTITIS, NO MALIGNANCY SEEN.; PLAIN ABDOMINAL RADIOGRAPHY: CHOLECYSTITIS

AE Stopped Rx Day	130
Duration of AE	22 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CHOLELITHIASIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

日本の治験責任医師からの報告。本被験者は4[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，胆管炎（総胆管結石）の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，クローン病，元喫煙者（1 日 15 本を 8 年間），腸切除，腸切除，胃食道逆流性疾患，高脂血症，胆石症及び元飲酒者（1 日 2～4 杯）であった。

投与 65 日後，被験者は胆管炎（総胆管結石）を発現した。投与 81 日後，胆管炎（総胆管結石）は消失した。

投与 65 日後，被験者は持続する発熱のため救急治療室を受診した。CT スキャンが行われ，胆管に結石が 1 つ認められた。同日，被験者は胆管炎と診断され，入院し，IV 抗生剤による治療を受けた。投与 67 日後，内視鏡的逆行性胆道膵管撮影（ERCP）及び内視鏡的乳頭括約筋切開が行われ，胆管から結石が除去された。投与 71 日後，被験者は下背部痛を訴え，胆石発作が疑われた。絶食が開始され，IV 抗生剤は継続された。投与 75 日後，CRP 及び肝機能検査値が低下したため，IV 抗生剤の投与は中止された。投与 81 日後，胆管炎が改善したと判断された後，被験者は退院した。

投与された薬剤は，アセリオ及びセフォンであった。

The patient’s past medications include:

REMICADE for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

AZANIN for CROHN'S DISEASE (20[redacted] - [redacted] 20[redacted])

HUMIRA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

STELARA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Cholangitis (10008604) (Cholangitis (10008604)) [v.22.1] [10008604]

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

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

Dechallenge: Not Applicable

2) Common bile duct stone (10010105) (Bile duct stone (10004637)) [v.22.1] [10010105]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of CHOLANGITIS, COMMON BILE DUCT STONE

- Investigator: Gallstone.

- AbbVie: Event more likely related to pre-existing gallstones. Prevalence of gallstones in the Japanese population is approximately 10%.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 144 U/L (normal 5 to 30)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 95 U/L (normal 5 to 30)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 54 U/L (normal 5 to 30)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 574 U/L (normal 117 to 356)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 453 U/L (normal 117 to 356)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 392 U/L (normal 117 to 356)

[redacted] **20[redacted] AMYLASE:** 73 U/L (normal 38 to 123)

[redacted] **20[redacted] AMYLASE:** 53 U/L (normal 38 to 123)

[redacted] **20[redacted] AMYLASE:** 98 U/L (normal 38 to 123)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 80 U/L (normal 11 to 30)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 44 U/L (normal 11 to 30)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 50 U/L (normal 11 to 30)

[redacted] **20[redacted] BILIRUBIN:** 2.3 mg/dL (normal 0.3 to 1.3)

[redacted] **20[redacted] BILIRUBIN:** 1.0 mg/dL (normal 0.3 to 1.3)

[redacted] **20[redacted] BILIRUBIN:** 0.5 mg/dL (normal 0.3 to 1.3)

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

[redacted] **20[redacted] C REACTIVE PROTEIN:** 11.50 mg/dL (normal 0 to 0.1)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 6.80 mg/dL (normal 0 to 0.1)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 5.17 mg/dL (normal 0 to 0.1)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 0.09 mg/dL (normal 0 to 0.1)

[redacted] **20[redacted] CT SCAN:** Suspected gallstone in the cystic duct.

[redacted] **20[redacted] CT SCAN:** Common bile stone was pointed out.

[redacted] 20[redacted] FECAL OCCULT BLOOD TEST: Negative

[redacted] **20[redacted] GGT:** 233 U/L (normal 12 to 50)

[redacted] **20[redacted] GGT:** 174 U/L (normal 12 to 50)

[redacted] **20[redacted] GGT:** 69 U/L (normal 12 to 50)

[redacted] **20[redacted] MRI:** COMMON BILE DUCT STONE

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4600 10^3/uL (normal 3600 to 9200)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3760 10^3/uL (normal 3600 to 9200)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3540 10^3/uL (normal 3600 to 9200)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3990 10^3/uL (normal 3600 to 9200)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

日本の治験責任医師からの報告。本被験者は 4[redacted] 歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，急性胆嚢炎の事象を発現した。

Event 3 の臨床経過：

関連する病歴は，クローン病，元喫煙者（1 日 15 本を 8 年間），腸切除，腸切除，胃食道逆流性疾患，静脈血栓症，高脂血症，IBS，胆石症及び元飲酒者（1 日 2～4 杯）であった。

投与 109 日後，被験者は急性胆嚢炎を発現した。投与 130 日後，急性胆嚢炎は消失した。

本事象発現前の投与 62 日後から投与 81 日後まで，被験者は胆管炎及び総胆管結石を発現し，AER #[redacted] に報告された。投与 94 日後，被験者は胆石発作のため救急治療室を受診した。胆石発作はアセリオの投与により緩和された。

投与 109 日後，被験者はアセリオの投与で緩和されなかった胆石発作による腹痛のため救急治療室を受診した。被験者は急性胆嚢炎と診断され，同日，入院した。被験者は抗生剤の静脈内投与，並びに断食及び補液療法による治療を受けた。投与 112 日後，被験者は胆嚢切除を受けた。投与 113 日後，IV 抗生剤は終了した。投与 120 日後，被験者の術後の経過は良好であったため，被験者は治験薬の静脈内投与を受けた。投与 130 日後，治験責任医師は急性胆嚢炎が回復したと判断し，被験者は退院した。

投与された薬剤は，ブスコパン，ジクロフェナク，ソセゴン，セフォン，アセリオ，フェンタニル，ソルデム 3A，ロキソプロフェン及びセレコックスであった。

The patient’s past medications include:

REMICADE for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

LIXIANA for THROMBOPROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

STELARA for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

ACELIO for CHOLANGITIS and CHOLELITHIASIS ([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 RISANKIZUMAB (Blinded)

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1) Acute cholecystitis (10000691) (Cholecystitis acute (10008614)) [v.23.1] [10000691]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of ACUTE CHOLECYSTITIS

- Investigator: cholelithiasis

- AbbVie: Risk factors includes pre-existing history of cholelithiasis, hyperlipidemia, and pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL ULTRASOUND: Stone in gallbladder neck

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 50 U/L (normal 5 to 30)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 32 U/L (normal 5 to 30)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 23 U/L (normal 5 to 30)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 33 U/L (normal 5 to 30)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 70 U/L (normal 5 to 30)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 405 U/L (normal 117 to 356)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 368 U/L (normal 117 to 356)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 251 U/L (normal 117 to 356)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 248 U/L (normal 117 to 356)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 333 U/L (normal 117 to 356)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 350 U/L (normal 117 to 356)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 36 U/L (normal 11 to 30)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 36 U/L (normal 11 to 30)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 44 U/L (normal 11 to 30)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 37 U/L (normal 11 to 30)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 30 U/L (normal 11 to 30)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 32 U/L (normal 11 to 30)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 49 U/L (normal 11 to 30)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 0.30 mg/dL (normal 0.1 to 50)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 3.90 mg/dL (normal 0.1 to 50)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 7.38 mg/dL (normal 0.1 to 50)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 0.81 mg/dL (normal 0.1 to 50)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 0.28 mg/dL (normal 0.1 to 50)

[redacted] **20[redacted] CT SCAN:** Stone in the gallbladder neck.

[redacted] **20[redacted] GGT:** 31 U/L (normal 12 to 50)

[redacted] **20[redacted] GGT:** 31 U/L (normal 12 to 50)

[redacted] **20[redacted] GGT:** 21 U/L (normal 12 to 50)

[redacted] **20[redacted] GGT:** 21 U/L (normal 12 to 50)

[redacted] **20[redacted] GGT:** 30 U/L (normal 12 to 50)

[redacted] **20[redacted] GGT:** 42 U/L (normal 12 to 50)

[redacted] **20[redacted] HISTOPATHOLOGY:** Acute cholecystitis, no malignancy seen.

[redacted] 20[redacted] PLAIN ABDOMINAL RADIOGRAPHY: Cholecystitis

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7910 uL (normal 3600 to 9200)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11660 uL (normal 3600 to 9200)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8110 uL (normal 3600 to 9200)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4810 uL (normal 3600 to 9200)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4810 uL (normal 3600 to 9200)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5340 uL (normal 3600 to 9200)

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
クローン病	X			

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO / P2:RZB 1200 MG IV	3[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: ALLERGIC RHINITIS	Not reported.
CROHN'S DISEASE	20[redacted]
OTHER: OLD PLEURITIS	20[redacted]
OTHER: INSOMNIA	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 54	54
Risankizumab	1200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 80	[redacted]20[redacted] / 136	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BCG Vaccine	Not reported.	Not reported.	Y-M: 19[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	75 mg	QD	Y-M: 20[redacted]
CLOSTRIDIUM BUTYRICUM	2 OTHER: TABLETS	TID	Y-M: 20[redacted]

VEDOLIZUMAB	300 mg	OTHER: ONCE PER 0WEEK,2WEEKS,6WEEKS.	Y-M: 20[redacted]
VEDOLIZUMAB	108 mg	OTHER: EVERY WEEK	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: ONCE PER 0WEEK,2WEEKS,6WEEKS	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: EVERY 4WEEKS	Y-M: 20[redacted]
USTEKINUMAB	390 mg	OTHER: ONCE	Y-M: 20[redacted] / -360
USTEKINUMAB	90 mg	OTHER: EVERY 7WEEKS	Y-M: 20[redacted] / -306
AMINO ACIDS NOS W/CARBOHYDRATES NOS	160 g	QD	Y-M: 20[redacted] / -236
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted] / -236
IRON	80 mg	OTHER: EVERY WEEK	Y-M: 20[redacted] / -133
MECOBALAMIN	500 mg	QD	Y-M: 20[redacted] / -84
LOPERAMIDE	0.5 mg	BID	Y-M: 20[redacted] / -56
METRONIDAZOLE	250 mg	BID	Y-M: 20[redacted] / -56
BROTIZOLAM	0.25 mg	QD	Y-M: 20[redacted] / -28
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -10
DIAZEPAM	10 mg	QD	Y-M: 20[redacted] / -9
DOMPERIDONE	5 mg	QD	Y-M: 20[redacted] / -9
HYOSCINE	10 mg	QD	Y-M: 20[redacted] / -9
MAGNESIUM CITRATE	100 g	QD	Y-M: 20[redacted] / -9
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / -9
SOLULACT S	500 mL	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
BCG Vaccine	Not reported.	Not reported.	Y-M: 19[redacted]	Not reported.
CLOSTRIDIUM BUTYRICUM	2 OTHER: TABLETS	TID	Y-M: 20[redacted]	ONGOING
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted] / -236	ONGOING
AMINO ACIDS NOS W/CARBOHYDRATES NOS	160 g	QD	Y-M: 20[redacted] / -236	Y-M: 20[redacted] / 44
MECOBALAMIN	500 mg	QD	Y-M: 20[redacted] / -84	ONGOING
METRONIDAZOLE	250 mg	BID	Y-M: 20[redacted] / -56	ONGOING
LOPERAMIDE	0.5 mg	BID	Y-M: 20[redacted] / -56	Y-M: 20[redacted] / 38
BROTIZOLAM	0.25 mg	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / 14

SOLULACT S	500 mL	QD	Y-M: 20[redacted] / 39	Y-M: 20[redacted] / 39
LOPERAMIDE	1 mg	TID	Y-M: 20[redacted] / 39	Y-M: 20[redacted] / 54
OSMOSAL	1000 mL	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 43
SOLULACT S	1000 mL	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 44
LYO-DIAMIN	10 mL	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 77
OSMOSAL	500 mL	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 48
SOLULACT S	500 mL	QD	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 48
CODEINE	2 g	TID	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 52
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / 46	ONGOING
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 48
CEFOTAXIME	1 g	TID	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 69
VANCOMYCIN	0.5 g	BID	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 71
OSMOSAL	1000 mL	QD	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 52
SOLULACT S	1000 mL	QD	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 52
VALACICLOVIR	500 mg	BID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 56
VIDARABINE	ADEQUATE g	BID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 73
SOLULACT S	500 mL	QD	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 71
OSMOSAL	500 mL	QD	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 77
LOPERAMIDE	1 g	TID	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 97
IRON	80 mg	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 71
MICONAZOLE	ADEQUATE g	TID	Y-M: 20[redacted] / 74	ONGOING
DIAZEPAM	10 mg	QD	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 80
DOMPERIDONE	5 mg	QD	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 80
HYOSCINE	10 mg	QD	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 80

MAGNESIUM CITRATE	100 g	QD	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 80
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 80
SOLULACT S	500 mL	QD	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 80
LOPERAMIDE	1 g	BID	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 119
ECABET	1.5 g	BID	Y-M: 20[redacted] / 113	ONGOING
LOPERAMIDE	1 g	TID	Y-M: 20[redacted] / 120	ONGOING
INFLUENZA VACCINE	0.5 mL	QD	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 124
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 163	Y-M: 20[redacted] / 163
DIAZEPAM	7.5 mg	QD	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 164
DOMPERIDONE	5 mg	QD	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 164
HYOSCINE	10 mg	QD	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 164
MAGNESIUM CITRATE	100 g	QD	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 164
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 164
SOLULACT S	500 mL	QD	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 164

Event #1: Serious Adverse Event

Event Description	WORSENING OF CROHN'S DISEASE
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 42
Age at AE Onset	3[redacted]

Laboratory Testing

Not reported

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 20): ABDOMINAL XP: NO ABNORMAL FINDING

AE Stopped Rx Day	164 (28 DAYS AFTER LAST TREATMENT)
Duration of AE	123 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INADEQUATE RESPONSE OF IP

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

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

日本の治験責任医師からの報告。本被験者は3[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，クローン病悪化の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，非喫煙者及び非飲酒者であった。

投与 42 日後，被験者はクローン病悪化を発現した。投 164 日後，クローン病悪化は消失した。

投与 39 日後，被験者は下痢，全身性疲労及び軽度の発熱を発現した。

投与 42 日後，被験者は入院した。入院中，被験者のクローン病症状は安定しており，重症度は中等度であることが判明した。投与 78 日後，被験者は退院した。

投与された薬剤は，ゼンタコート，コデインリン酸塩，ソルラクト S 及びロペラミド塩酸塩であった。

The patient’s past medications include:

IMURAN for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted])

AZANIN for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted])

VEDOLIZUMAB for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted], [redacted]20[redacted] - [redacted]20[redacted])

REMICADE for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted], [redacted]20[redacted] - [redacted]20[redacted])

STELARA for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted], [redacted]20[redacted] - [redacted]20[redacted])

FESIN for CROHN'S DISEASE ([redacted]20[redacted] - [redacted]20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Crohn's disease aggravated (10011403) (Crohn's disease (10011401)) [v.22.1] [10011403]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of WORSENING OF CROHN'S DISEASE

- Investigator: Inadequate response of IP

- AbbVie: Event is more likely related to pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL X-RAY: No abnormal finding

[redacted] **20[redacted] ILEOCOLONOSCOPY:** No biopsies taken, however results from scope not provided

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
腹痛	X			
クローン病	X			

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	7[redacted]	MALE	ASIAN

Medical History	Onset Year
BENIGN PROSTATIC HYPERPLASIA	Not reported.
LATENT TUBERCULOSIS	Not reported.
CROHN'S DISEASE	20[redacted]
TUBERCULOSIS: LATENT TUBERCULOSIS	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 23	23

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]
ISONIAZID	300 mg	QD	Y-M: 20[redacted]
PYRIDOXINE	50 mg	QD	Y-M: 20[redacted]
RIFAMPICIN	600 mg	QD	Y-M: 20[redacted]

BCG Vaccine	Not reported.	Not reported.	Y-M: 20
DUTASTERIDE	0.5 mg	QD	Y-M: 20
IMIDAFENACIN	0.1 mg	BID	Y-M: 20
TERAZOSIN	5 mg	QD	Y-M: 20
MESALAZINE	2 g	BID	Y-M: 20
TRIMEBUTINE	300 mg	BID	Y-M: 20
FOLIC ACID	1 mg	QD	Y-M: 20
HYDROCORTISONE	100 mg	OTHER: Q2W	Y-M: 20
INFLIXIMAB	300 mg	OTHER: Q2W	Y-M: 20
HYDROCORTISONE	100 mg	OTHER: Q4W	Y-M: 20
INFLIXIMAB	300 mg	OTHER: Q4W	Y-M: 20
HYDROCORTISONE	100 mg	OTHER: Q2M	Y-M: 20
INFLIXIMAB	300 mg	OTHER: Q2M	Y-M: 20
METHOTREXATE	15 mg	OTHER: Q2M(8DAYS)	Y-M: 20
INFLIXIMAB	600 mg	OTHER: Q2M	Y-M: 20
REBAMIPIDE	100 mg	BID	Y-M: 20
MOVPREP	2 L	OTHER: ONCE	Y-M: 20 / -19
SIMETICONE	600 mg	OTHER: ONCE	Y-M: 20 / -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
ESOMEPRAZOLE	40 mg	QD	Y-M: 20	ONGOING
BCG Vaccine	Not reported.	Not reported.	Y-M: 20	Not reported.
DUTASTERIDE	0.5 mg	QD	Y-M: 20	ONGOING
IMIDAFENACIN	0.1 mg	BID	Y-M: 20	ONGOING
TERAZOSIN	5 mg	QD	Y-M: 20	ONGOING
MESALAZINE	2 g	BID	Y-M: 20	ONGOING
TRIMEBUTINE	300 mg	BID	Y-M: 20	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20	ONGOING
METHOTREXATE	15 mg	OTHER: Q2M(8DAYS)	Y-M: 20	ONGOING
REBAMIPIDE	100 mg	BID	Y-M: 20	ONGOING
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 OTHER: T	TID	Y-M: 20 / 20	Y-M: 20 / 22
TRAMADOL	100 mg	BID	Y-M: 20 / 29	ONGOING
PROPACETAMOL	1 g	QD	Y-M: 20 / 31	Y-M: 20 / 31
TRAMADOL	50 mg	QD	Y-M: 20 / 31	Y-M: 20 / 31
VITAMINS NOS	5 mL	QD	Y-M: 20 / 31	Y-M: 20 / 31
SMOFKABIVEN PERIFER	1448 mL	QD	Y-M: 20 / 31	Y-M: 20 / 32

CEFTRIAXONE	2 g	QD	Y-M: 20[redacted]-[redacted] / 31	Y-M: 20[redacted]-[redacted] / 33
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]-[redacted] / 31	Y-M: 20[redacted]-[redacted] / 34
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted]-[redacted] / 31	Y-M: 20[redacted]-[redacted] / 36
HYDROCORTISONE	80 mg	TID	Y-M: 20[redacted]-[redacted] / 32	Y-M: 20[redacted]-[redacted] / 34
ALANINE W/ARGININE/CALCIUM CHLORIDE	1085 mL	QD	Y-M: 20[redacted]-[redacted] / 32	Y-M: 20[redacted]-[redacted] / 35
MIRABEGRON	50 mg	QD	Y-M: 20[redacted]-[redacted] / 32	Y-M: 20[redacted]-[redacted] / 36
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]-[redacted] / 34	ONGOING
LIVALAVIN	1 mL	QD	Y-M: 20[redacted]-[redacted] / 36	Y-M: 20[redacted]-[redacted] / 36

Event #1: Serious Adverse Event

Event Description	WORSENING OF ABDOMEN PAIN, RELATED TO CROHN'S DISEASE
Preferred term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 18
Age at AE Onset	7[redacted]
Laboratory Testing	
Not reported	
Microbiology	
Not reported	
SAE Supplemental Procedure	
Not reported	
AE Stopped Rx Day	23
Duration of AE	6 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN'S DISEASE AGGRAVATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	WORSENING OF ABDOMEN PAIN, RELATED TO CROHN'S DISEASE
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 18
Age at AE Onset	7[redacted]

Laboratory Testing
Not reported
Microbiology
Not reported
SAE Supplemental Procedure
Not reported

AE Stopped Rx Day	23
Duration of AE	6 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN'S DISEASE AGGRAVATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	WORSENING OF ABDOMEN PAIN, RELATED TO CROHN'S DISEASE
Preferred term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 29 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 31): Alanine Aminotransferase: 19 [5 - 46] IU/L; Albumin: 3.8 [3.3 - 5.3] g/dL; Alkaline Phosphatase: 101 [50 - 151] IU/L; Aspartate Aminotransferase: 14 [13 - 34] IU/L; Basophils/Leukocytes: 0.3 [0 - 1.5] %; Bilirubin: 1.3 [0.5 - 1.8] mg/dL; Blood Urea Nitrogen: 18.9 [8.5 - 22] mg/dL; C Reactive Protein: 106.6 [0 - 8] mg/L; Calcium: 8.7 [8.5 - 10.5] mg/dL; Cholesterol: 115 [142 - 240] mg/dL; Creatinine: 0.75 [0.68 - 1.19] mg/dL; Eosinophils/Leukocytes: 0.05 [0 - 0.5] %; Ery. Mean Corpuscular Hemoglobin: 28.7 [27 - 33.1] pg; Ery. Mean Corpuscular Volume: 83.6 [80 - 98] fL; Erythrocytes: 4.15 [4.4 - 6.1] 10^6/uL; Glucose: 122 [70 - 110] mg/dL; Hematocrit: 34.7 [40 - 52] %; Leukocytes: 11.75 [4 - 10.8] 10^3/uL; Lymphocytes/Leukocytes: 6.1 [19 - 51] %; Monocytes/Leukocytes: 8.3 [3.3 - 10.8] %; Neutrophils/Leukocytes: 84.9 [39 - 74] %; Phosphate: 3.0 [2.5 - 4.2] mg/dL; Platelets: 249 [150 - 400] 10^3/uL; Protein: 6.2 [6 - 8] g/dL; Urate: 3.8 [3.5 - 8.1] mg/dL

Microbiology
Not reported
SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 10): CT ABD+PEL (CONTRAST): AGGRAVATED WALL THICKENING AND ENHANCEMENT INVOLVING TERMINAL AND DISTAL ILEUM WITH PERIENTERIC FAT STRANDINGS AND COMB SIGN, SUGGESTING OF AGGRAVATION OF ACTIVE CROHN'S DISEASE.

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN'S DISEASE AGGRAVATION
Discontinued Study Drug Due to the Event	NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted] 20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

韓国の治験責任医師からの報告。本被験者は 7[redacted] 歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，腹痛悪化（クローン病に関連あり）の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，クローン病，潜伏結核，非喫煙者，現飲酒者（1 日 2 杯未満）及び良性前立腺肥大症であった。

投与 20 日後，被験者は腹痛悪化（クローン病に関連あり）を発現した。投与 23 日後，腹痛悪化（クローン病に関連あり）は消失した。

投与 20 日後，被験者はクローン病に関連する腹痛悪化のため入院した。投与 22 日後，症状が改善し，被験者は退院した。

投与された薬剤は，Tridol 及び Alusilsan であった。

The patient's past medications include:

CORTISOLU for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

REMSIMA for CROHN'S DISEASE ([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 RISANKIZUMAB (Blinded)

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1) Abdominal pain aggravated (10048358) (Abdominal pain (10000081)) [v.23.0] [10048358]

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

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

Dechallenge: Not Applicable

2) Crohn's disease (10011401) (Crohn's disease (10011401)) [v.23.0] [10011401]

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

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

Dechallenge: Not Applicable

Alternative Etiology forRISANKIZUMAB (Blinded)

Event of WORSENING OF ABDOMEN PAIN, RELATED TO CROHN'S DISEASE

- Investigator: Crohn's disease aggravation.

- AbbVie: Event more likely due to pre-existing Crohn's disease.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

韓国の治験責任医師からの報告。本被験者は 7[redacted] 歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，腹痛悪化（クローン病に関連あり）の事象を発現した。

Event 3 の臨床経過：

関連する病歴は，クローン病，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

投与 29 日後，被験者は腹痛悪化（クローン病に関連あり）を発現した。

入院前の投与 20 日後，クローン病に関連する腹痛悪化が始まり，被験者は投与 20 日後から投与 22 日後まで入院した（AER: [redacted]）。投与 23 日後，本事象のため治験薬の投与は中止され，再開はされなかった。投与 30 日後，被験者は血便排泄を発現した。

投与 31 日後，被験者は入院し，治験の同意撤回を決断した。被験者は疼痛管理の目的で入院を希望した。入院中，保存療法及び疼痛管理が行われた。

投与された薬剤は，トラマドール塩酸塩，Alusilsan，Solondo，Cortisolu，Metrynal，Denogan，Tridol 及びセフトリアキソンであった。

The patient’s past medications include:

CORTISOLU for CROHN'S DISEASE ([redacted])

REMSIMA for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Abdominal pain aggravated (10048358) (Abdominal pain (10000081)) [v.23.0] [10048358]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of WORSENING OF ABDOMEN PAIN, RELATED TO CROHN'S DISEASE

- **Investigator:** Crohn's Disease Aggravated.

- **AbbVie:** Event more likely related to pre-existing Crohn's Disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **CT ABDOMEN AND PELVIS WITH CONTRAST:** Aggravated wall thickening and enhancement involving terminal and distal ileum with perienteric fat strandings and comb sign, suggesting of aggravation of active Crohn's 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
網膜障害	X			

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO / P2:RZB 1200 MG IV	5[redacted]	MALE	WHITE

Medical History	Onset Year
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: GASTRODUODENITIS CHRONICA	20[redacted]
CROHN'S DISEASE	20[redacted]
ANEMIA: SIDEROPENIC ANEMIA DUE TO ACTIVE CROHN'S DISEASE	20[redacted]

Prior Procedures	Procedure Year
SURGERY: SURGICAL PROCEDURE DUE TO FRACTURE OF LEFT FEMURE IN CAR ACCIDENT	19[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): BIOPSY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
Risankizumab	1200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 84	[redacted]20[redacted] / 140	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BCG Vaccine	Not reported.	Not reported.	Y-M: 19[redacted]
MESALAZINE	3 g	QD	Y-M: 20[redacted] / -235
METHOTREXATE	25 mg	OTHER: ONCE A WEEK	Y-M: 20[redacted] / -222
BUDESONIDE	2 mg	QD	Y-M: 20[redacted] / -124
LOPERAMIDE	2 mg	TID	Y-M: 20[redacted] / -29
MOVIPREP	1 L	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
BCG Vaccine	Not reported.	Not reported.	Y-M: 19[redacted]	Not reported.
MESALAZINE	3 g	QD	Y-M: 20[redacted] / -235	ONGOING
METHOTREXATE	25 mg	OTHER: ONCE A WEEK	Y-M: 20[redacted] / -222	ONGOING
LOPERAMIDE	2 mg	TID	Y-M: 20[redacted] / -29	ONGOING
TOBRAMYCIN	1 gtt	QID	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 193

Event #1: Serious Adverse Event

Event Description	RETINAL ABLATION OF THE LEFT EYE
Preferred term	網膜障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 140
Age at AE Onset	5[redacted]
Laboratory Testing	
Not reported	
Microbiology	
Not reported	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx Day 133): PHACOEMULSIFICATION WITH INTRAOCULAR LENS IMPLANTATION AND PARS PLANA VITRECTOMY: PATIENT HAS RECOVERED	
AE Stopped Rx Day	144 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CONCOMITANT DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

クロアチアの治験責任医師からの報告。本被験者は5[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，左眼の網膜剥離の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，元喫煙者（1 日 1 箱を 20 年間）及び過去のアルコール摂取（1 日 2 杯未満）であった。

投与 140 日後，被験者は左眼の網膜剥離を発現した。投与 144 日後，左眼の網膜剥離は消失した。

投与 140 日後，被験者は Week 20 来院を行い，左眼の視野にぼやけた場所があると訴えた。被験者は眼科医の検査を受け，左眼の網膜剥離と診断された。投与 141 日後，被験者は外科治療の

ため入院した。水晶体乳化及び眼内レンズ挿入，並びに経毛様体扁平部硝子体切除が行われ，合併症は認められなかった。投与 144 日後，被験者は退院した。

投与された薬剤は，トブラマイシンであった。

The patient’s past medications include:

BUDESONIDE for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Retinal disorder (10038853) (Retinal disorder (10038853)) [v.24.0] [10038853]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of RETINAL ABLATION OF THE LEFT EYE

- Investigator: Concomitant disease

- AbbVie: Risk factor includes age greater than 50 years old in a setting of pre-existing Crohn's 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
肝機能異常	X	X		X
発疹	X	X		
** (ALT > 3 × ULN or AST > 3 × ULN) with Tbili ≥in 2 × ULN using lab data				X
** ALT ≥in 5 × ULN using lab data				X
** AST ≥in 5 × ULN using lab data				X

Treatment Group	Age at Study Start	Sex	Race
P1:RZB 600 MG IV	3[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: ANAL FISTULA	20[redacted]
OTHER: THE ECG AXIS IS SIGNIFICANTLY SKEWED TO THE LEFT	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: EXTREME RIGHT DEVIATION OF ELECTRIC SHAFT	20[redacted]
LIVER DISEASE (EXCLUDING HEPATITIS): DIFFUSE MILD FATTY LIVER	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 29	29

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
OTHER NUTRIENTS	2000 mL	QD	Y-M: 20[redacted]
OTHER NUTRIENTS	400 g	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
OTHER NUTRIENTS	320 g	QD	Y-M: 20[redacted]
AZATHIOPRINE	125 mg	QD	Y-M: 20[redacted] / -202
OTHER NUTRIENTS	APPROPRIATE g	QD	Y-M: 20[redacted] / -50
COLOPEG	205.68 g	QD	Y-M: 20[redacted] / -11
PROPOFOL	UNKNOW mL	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
AZATHIOPRINE	125 mg	QD	Y-M: 20[redacted] / -202	Y-M: 20[redacted] / 80
OTHER NUTRIENTS	APPROPRIATE g	QD	Y-M: 20[redacted] / -50	ONGOING
OTHER NUTRIENTS	UNKNOWN g	OTHER: UNKNOWN	Y-M: 20[redacted] / 73	Y-M: 20[redacted] / 225
ERGOCALCIFEROL;PHYTOMENADIONE;RETINOL;VITAMIN	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 87
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 87
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 87
POTASSIUM	1 g	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 87
GLYCYRRHIZIC ACID	100 mg	QD	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 87
PHOSPHATIDYL CHOLINE	465 mg	QD	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 87
ESOMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 106
GLYCYRRHIZIC ACID	150 mg	TID	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 106
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 106
PHOSPHATIDYL CHOLINE	0.456 g	TID	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 106
METHYLPREDNISOLONE	12 mg	QD	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 123

Event #1: AE Leading to Discontinuation of Study Drug

Event Description	RASH

Preferred term	発疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 55 (26 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
Not Applicable	
Microbiology	
Not Applicable	
SAE Supplemental Procedure	
Not Applicable	
AE Stopped Rx Day	61 (32 DAYS AFTER LAST TREATMENT)
Duration of AE	7 DAYS
Severity	Mild
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	Not Applicable
Discontinued Study Drug Due to the Event	YES
SAE Criteria	None

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

Event Description	RASH
Preferred term	発疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 80 (51 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
[redacted]20[redacted] (Rx Day 82): C Reactive Protein: 22.28 [0 - 3] mg/L; Creatinine: 58.58 [44 - 133] umol/L; Leukocytes: 5.590 [4 - 10] 10^9/L; NPTST054-C-REACTIVE PROTEIN: 21.36 [0 - 10] mg/L; NPTST054-C-REACTIVE PROTEIN: 27.31 [0 - 10] mg/L; Neutrophils: 5.070 [2 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 109): NPTST054-C-REACTIVE PROTEIN: 0.56 [0 - 10] mg/L	
Microbiology	
Not reported	
SAE Supplemental Procedure	
Not reported	
AE Stopped Rx Day	109 (80 DAYS AFTER LAST TREATMENT)
Duration of AE	30 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	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Hepatic Events

Event Description	DAMAGE OF HEPATIC FUNCTION
Preferred term	肝機能異常

AE Onset Date / Rx Day [redacted]20[redacted] / 82 (53 DAYS AFTER LAST TREATMENT)
Age at AE Onset 3[redacted]
Laboratory Testing
[redacted]20[redacted] (Rx Day -20): Alanine Aminotransferase: 7 [6 - 43] U/L; Alkaline Phosphatase: 86 [31 - 129] U/L; Aspartate Aminotransferase: 15 [11 - 36] U/L; Bilirubin: 19 [3 - 21] umol/L; NPTST081-DIR BILI: 5 [Not reported - 7] umol/L; NPTST115-GGT: 19 [10 - 61] U/L; [redacted]20[redacted] (Rx Day 82): Alanine Aminotransferase: 2155 [3 - 35] U/L; Alanine Aminotransferase: 1965.89 [0 - 40] U/L; Alkaline Phosphatase: 114.67 [0 - 240] U/L; Aspartate Aminotransferase: 900.25 [0 - 40] U/L; Aspartate Aminotransferase: 1198 [15 - 40] U/L; Bilirubin: 46.19 [5 - 21] umol/L; Bilirubin: 44.64 [5 - 21] umol/L; C Reactive Protein: 22.28 [0 - 3] mg/L; Creatinine: 58.70 [44 - 133] umol/L; Creatinine: 58.58 [44 - 133] umol/L; Eosinophils/Leukocytes: 0.004 [0.005 - 0.05] Unit not reported; Eosinophils/Leukocytes: 0.002 [0.005 - 0.05] Unit not reported; Glucose: 11.17 [3.89 - 6.11] mmol/L; Hematocrit: 0.451 [0.35 - 0.45] Unit not reported; Leukocytes: 5.590 [4 - 10] 10^9/L; Lymphocytes: 0.460 [0.8 - 4] 10^9/L; Lymphocytes/Leukocytes: 0.082 [0.2 - 0.4] Unit not reported; Monocytes/Leukocytes: 0.007 [0.03 - 0.1] Unit not reported; NPTST023-APOB: 0.47 [0.63 - 1.88] g/L; NPTST024-APTT: 33.2 [25.1 - 36.5] sec; NPTST054-C-REACTIVE PROTEIN: 21.36 [0 - 10] mg/L; NPTST079-DBIL: 13.36 [0 - 3.4] umol/L; NPTST079-DBIL: 13.84 [0 - 3.4] umol/L; NPTST122-HBCAB: 14.18 [0 - 1] Unit not reported; NPTST124-HBSAB: 11.37 [0 - 10] Unit not reported; NPTST127-HCV-AB: 0.024 [0 - 1] Unit not reported; NPTST139-HIV: 0 [0 - 1] Unit not reported; NPTST141-IBIL: 32.35 [5 - 17.6] umol/L; NPTST141-IBIL: 31.28 [5 - 17.6] umol/L; NPTST145-INORGANIC PHOSPHORUS: 0.61 [0.83 - 1.96] mmol/L; NPTST146-INR: 1.37 [0.8 - 1.2] Unit not reported; NPTST168-MEAN CORPUSCULAR HEMOGLOBIN: 33.800 [27 - 31] pg; NPTST200-PREALBUMIN: 0.19 [0.2 - 0.4] g/L; NPTST207-PT: 14.6 [9.4 - 12.5] sec; NPTST210-R-GLUTAMYL TRANSPEPTIDASE: 106.90 [0 - 60] U/L; NPTST226-RETINOL BINDING PROTEIN WAS DET: 18.70 [25 - 70] mg/L; NPTST259-TOTAL BILE ACID: 17.74 [0 - 10] umol/L; NPTST261-TOTAL IGE: 55.50 [0 - 60] Unit not reported; NPTST278-URINE LIQUID SILK: POSITIVE [Not reported - Not reported] Unit not reported; NPTST281-UROBILINOGEN: 1+ [1.005 - 1.03] Unit not reported; Neutrophils: 5.070 [2 - 7.5] 10^9/L; Neutrophils/Leukocytes: 0.907 [0.5 - 0.75] Unit not reported; Occult Blood: WEAK POSITIVE [Not reported - Not reported] Unit not reported; [redacted]20[redacted] (Rx Day 85): Alanine Aminotransferase: 742.66 [0 - 40] U/L; Albumin: 35.66 [40 - 55] g/L; Aspartate Aminotransferase: 87.02 [0 - 40] U/L; [redacted]20[redacted] (Rx Day 87): Alanine Aminotransferase: 431.99 [0 - 40] U/L; Albumin: 36.50 [40 - 55] g/L; Aspartate Aminotransferase: 44.95 [0 - 40] U/L; [redacted]20[redacted] (Rx Day 92): Alanine Aminotransferase: 143 [3 - 35] U/L; Aspartate Aminotransferase: 29 [15 - 40] U/L; [redacted]20[redacted] (Rx Day 93): Bilirubin: 37.18 [5 - 21] umol/L; NPTST016-ANTI-HEPATOCYTE CYTOPLASMIC ANT: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST017-ANTI-LIVER AND KIDNEY MICROSOMA: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST018-ANTI-MITOCHONDRIAL ANTIBODY (AM: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST019-ANTI-MITOCHONDRIAL M2-TYPE ANTI: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST020-ANTI-SOLUBLE LIVER ANTIGEN ANTI: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST021-ANTIPROMYELOCYTIC LEUKEMIA PROT: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST121-HAV-IGM: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST123-HBCAB-IGM: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST125-HBV-DNA: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST128-HCV-AG: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST129-HCV-IGG: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST136-HEV-IGG: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST137-HEV-IGM: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST219-RESISTANCE TO GP210 ANTIBODY: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST220-RESISTANCE TO SP100 ANTIBODY: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST227-RO - 52 ANTIBODIES: NEGATIVE [Not reported - Not reported] Unit not reported; [redacted]20[redacted] (Rx Day 109): Alkaline Phosphatase: 57 [31 - 129] U/L; Alkaline Phosphatase: 61.46 [0 - 240] U/L; [redacted]20[redacted] (Rx Day 132): Alanine Aminotransferase: 65 [3 - 35] U/L; Aspartate Aminotransferase: 29 [15 - 40] U/L; [redacted]20[redacted] (Rx Day 150): Alanine Aminotransferase: 39 [3 - 35] U/L; Aspartate Aminotransferase: 25 [15 - 40] U/L

Microbiology	
Not reported	
SAE Supplemental Procedure	
Not reported	
AE Stopped Rx Day	150 (121 DAYS AFTER LAST TREATMENT)
Duration of AE	69 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	Not reported
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

中国の治験責任医師からの報告。本被験者は3[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，肝機能障害及び発疹の事象を発現した。

Event 2 及び 3 の臨床経過：

関連する病歴は，クローン病，軽度のびまん性脂肪肝，非喫煙者及び非飲酒者であった。

投与 80 日後，被験者は発疹を発現した。投与 82 日後，被験者は肝機能障害を発現した。投与 109 日後，発疹は消失した。投与 150 日後，肝機能障害は消失した。

本事象発現前の投与の約 2 か月後，被験者はそう痒を伴う非重篤な皮疹と診断され，その時点で治験薬の投与は完全に中止された。発疹は治療を行うことなく自然消失した。

投与 82 日後，被験者は内太腿の皮疹のため入院した。内太腿の皮疹は徐々に悪化し，胸部や背部などの別の部位に散在する大型の斑状変化などが認められた。他の症状は認められなかった。病院の皮膚科医の診察が行われた。「膨疹」を伴う下肢の発疹及びそう痒などの所見が 2 日間認められた。身体的診察で，被験者の両腿には対称な薄片状の暗赤色斑点があり，膨疹は押すと部分的に消え，薄くなった。肝機能検査も完了し，肝機能上昇が認められた。リンパ節病変は認められなかった。肝臓保護のための治療が開始され，発疹に対してステロイドによる治

療が開始された。治療後，発疹及び肝機能は改善した。投与 87 日後，被験者は退院した。

被験者は新規薬剤，ハーブサプリメント，茶，レクリエーション薬物の使用及びアルコール摂取を否定した。特別な食べ物やキノコ摂取もなく，最近の発熱，関節痛，胸の苦しさ及び息切れもなかった。最近の職業性曝露，刺鍼法，刺青及び最近の国外旅行もなかった。被験者は肝臓疾患の家族歴も否定した。肝酵素増加及びアレルギーの治療歴及び既往もなかった。

投与された薬剤は，magnesium isoglycyrrhizinate，グリチルリチン酸二アンモニウム，メチルプレドニゾロン，ネキシウム，ポリエンホスファチジルコリン及び esomeprazole sodium であった。

The patient’s past medications include:

ENTERAL NUTRITIONAL EMULSION for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTERAL NUTRITIONAL POWDER for CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Hepatic function disorder (10019674) (Hepatic function abnormal (10019670)) [v.23.0] [10019674]

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

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

Dechallenge: Not Applicable

2) Rash (10037844) (Rash (10037844)) [v.23.0] [10037844]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of DAMAGE OF HEPATIC FUNCTION

- Investigator: Not Applicable

- AbbVie: The delayed time-to-event onset (7 weeks since last study drug dose), rapid resolution of AST and ALT in the setting of a long half-life when the study drug would be still pharmacologically active, and the lack of a safety concern for hepatotoxicity based on robust adverse event and lab data to date, make the causal association to the study drug unlikely.

Event of RASH

- Investigator: Not Applicable

- AbbVie: Common and nonspecific event term with multiple underlying etiologies. additional risk factor includes concurrent event of damage of hepatic function.Relevant Laboratory & Other Diagnostic Tests

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[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 7 U/L (normal 6 to 43)

[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 9 U/L (normal 6 to 43)

[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 1965.89 U/L (normal 0 to 40)

[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 2155 U/L (normal 0 to 40)

[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 742.66 U/L (normal 0 to 40)

[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 431.99 U/L (normal 0 to 40)

[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 143 U/L (normal 3 to 35)

[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 65 U/L (normal 3 to 35)

[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 39 U/L (normal 3 to 35)

[redacted] 20[redacted] ALBUMIN: 42.81 no unit

[redacted] **20[redacted] ALBUMIN:** 35.66 G/L (normal 40 to 55)

[redacted] **20[redacted] ALBUMIN:** 36.50 G/L (normal 40 to 55)

[redacted] **20[redacted] ALBUMIN BCG:** 44 G/L (normal 33 to 49)

[redacted] **20[redacted] ALBUMIN-BCG:** 44 G/L (normal 33 to 49)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 86 U/L (normal 31 to 129)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 114.67 U/L (normal 0 to 240)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 61.46 U/L (normal 0 to 240)

[redacted] 20[redacted] ALKALINE PHOSPHATASE-QT: 73 U/L (normal 31 to 129)

[redacted] 20[redacted] ALKALINE PHOSPHATASE-QT: 57 U/L (normal 31 to 129)

[redacted] 20[redacted] ANTI HEPATOCYTE CYTOPLASMIC ANTIGEN TYPE I ANTIBODY: Negative

[redacted] 20[redacted] ANTI LIVER AND KIDNEY MICROSOMAL ANTIBODY (LKM): Negative

[redacted] 20[redacted] ANTI-MITOCHONDRIAL ANTIBODY AMA-M2-3E: Negative

[redacted] 20[redacted] ANTI-MITOCHONDRIAL M2-TYPE ANTIBODY: Negative

[redacted] 20[redacted] ANTI-SOLUBLE LIVER ANTIGEN ANTIBODY (SLA/LP): Negative

[redacted] 20[redacted] ANTIPROMYELOCYTIC LEUKEMIA PROTEIN ANTIBODY: Negative

[redacted] **20[redacted] APOB:** 0.47 G/L (normal 0.63 to 1.88)

[redacted] **20[redacted] APTT:** 33.2 SEC (normal 25.1 to 36.5)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 15 U/L (normal 11 to 36)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 18 U/L (normal 11 to 36)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 900.25 U/L (normal 0 to 40)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 1198 U/L (normal 15 to 40)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 87.02 U/L (normal 0 to 40)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 44.95 U/L (normal 0 to 40)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 29 U/L (normal 15 to 40)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 29 U/L (normal 15 to 40)

[redacted] **20[redacted] BASOPHILS:** 0.03 G/L (normal 0.0 to 0.2)

[redacted] **20[redacted] BASOPHILS:** 0.01 X10**3/MCL (normal 0.00 to 0.20)

[redacted] **20[redacted] BASOPHILS %:** 0.6 % (normal 0.0 to 2.0)

[redacted] **20[redacted] BASOPHILS %:** 0.1 % (normal 0.0 to 2.0)

[redacted] **20[redacted] CALCIUM (EDTA):** 2.42 MMOL/L (normal 2.07 to 2.64)

[redacted] **20[redacted] CHOLESTEROL:** 2.85 MMOL/L (normal 3.88 to 6.83)

[redacted] 20[redacted] CHOLESTEROL: 3.07 no unit

[redacted] 20[redacted] CHOLESTEROL (HIGH PERFORMANCE): 7.62 MMOL/L (normal 3.86 to 6.83)

[redacted] **20[redacted] CREATININE:** 58.58 umol/L (normal 44 to 133)

[redacted] **20[redacted] CREATININE:** 58.70 umol/L (normal 44 to 133)

[redacted] 20[redacted] CREATININE (RATE BLANKED): 80 MCMOL/L (normal 40 to 110)

[redacted] **20[redacted] CRP:** 21.36 MG/L (normal 0 to 10)

[redacted] **20[redacted] CRP:** 27.31 MG/L (normal 0 to 10)

[redacted] **20[redacted] CRP:** 0.56 MG/L (normal 0 to 10)

[redacted] 20[redacted] DIRECT BILIRUBIN: 5 umol/L (normal 2 to 7)

[redacted] 20[redacted] DIRECT BILIRUBIN: 4 umol/L (normal 2 to 7)

[redacted] **20[redacted] DIRECT BILIRUBIN:** 13.36 umol/L (normal 0 to 3.4)

[redacted] **20[redacted] DIRECT BILIRUBIN:** 13.84 umol/L (normal 0 to 3.4)

[redacted] **20[redacted] DIRECT BILIRUBIN:** 5 MCMOL/L (normal 2 to 7)

[redacted] **20[redacted] DIRECT HDL:** 1.13 MMOL/L (normal 0.72 to 1.63)

[redacted] 20[redacted] DIRECT HDL-C 3RD GENERATION-QT: 3.39 MMOL/L (normal 0.72 to 1.63)

[redacted] **20[redacted] EOSINOPHILS:** 0.05 G/L (normal 0.0 to 0.57)

[redacted] **20[redacted] EOSINOPHILS:** 0.02 X10**3/MCL (normal 0.00 to 0.57)

[redacted] **20[redacted] EOSINOPHILS %:** 1 % (normal 0.0 to 6.8)

[redacted] **20[redacted] EOSINOPHILS %:** 0.004 % (normal 0.005 to 0.05)

[redacted] **20[redacted] EOSINOPHILS %:** 0.002 % (normal 0.005 to 0.05)

[redacted] **20[redacted] EOSINOPHILS %:** 0.3 % (normal 0.0 to 6.8)

[redacted] **20[redacted] EOSINOPHILS ABS:** 5.070 X10**9/L (normal 2 to 7.5)

[redacted] 20[redacted] GAMMA-GLUTAMYLTRANSFERASE: 19 U/L (normal 10 to 61)

[redacted] 20[redacted] GAMMA-GLUTAMYLTRANSFERASE: 21 U/L (normal 10 to 61)

[redacted] 20[redacted] GAMMA-GLUTAMYLTRANSFERASE: 101 U/L (normal 10 to 61)

[redacted] **20[redacted] GLUCOSE:** 11.17 MMOL/L (normal 3.89 to 6.11)

[redacted] 20[redacted] GP210 ANTIBODY RESISTANCE: Negative

[redacted] 20[redacted] HAV-IGM: Negative

[redacted] **20[redacted] HBCAB:** 14.18 COI (normal 0 to 1.0)

[redacted] 20[redacted] HBCAB-IGM: Negative

[redacted] 20[redacted] HBEAG: Negative

[redacted] **20[redacted] HBSAB:** 11.37 (No unit) (normal 0 to 10)

[redacted] 20[redacted] HBSAG: Negative

[redacted] **20[redacted] HBV DNA:** No HBV DNA detected

[redacted] 20[redacted] HBV DNA: Negative

[redacted] **20[redacted] HCT:** 0.41 no unit (normal 0.39 to 0.54)

[redacted] **20[redacted] HCT:** 0.451 no unit (normal 0.35 to 0.45)

[redacted] **20[redacted] HCV-AB:** 0.024 COI (normal 0 to 1.0)

[redacted] 20[redacted] HCV-AG: Negative

[redacted] 20[redacted] HCV-IGG: Negative

[redacted] **20[redacted] HEMATOCRIT:** 49 % (normal 39 to 54)

[redacted] **20[redacted] HEMOGLOBIN:** 134G/L (normal 127 to 181)

[redacted] **20[redacted] HEMOGLOBIN:** 15.5 G/DL (normal 12.7 to 18.1)

[redacted] 20[redacted] HEV-IGG: Negative

[redacted] 20[redacted] HEV-IGM: Negative

[redacted] 20[redacted] HIGH SENSITIVITY CRP: 22.28 MG/L (normal 0 to 3)

[redacted] **20[redacted] HIV:** 0 (normal 0 to 1.0)

[redacted] **20[redacted] INDIRECT BILIRUBIN:** 32.35 umol/L (normal 5 to 17.6)

[redacted] **20[redacted] INDIRECT BILIRUBIN:** 31.28 umol/L (normal 5 to 17.6)

[redacted] **20[redacted] INORGANIC PHOSPHORUS:** 0.61 MMOL/L (normal 0.83 to 1.96)

[redacted] **20[redacted] INR:** 1.37 no unit (normal 0.8 to 1.2)

[redacted] 20[redacted] LDL CHOL-FRIEDEWALD 3RD -QT: 3.21 MMOL/L (normal 2.02 to 4.78)

[redacted] 20[redacted] LOW DENSITY LIPOPROTEIN: 1 MMOL/L (normal 2.02 to 4.78)

[redacted] **20[redacted] LYMPHOCYTES:** 1.11 G/L (normal 0.91 to 4.28)

[redacted] **20[redacted] LYMPHOCYTES:** 0.93 X10**3/MCL (normal 0.91 to 4.28)

[redacted] **20[redacted] LYMPHOCYTES %:** 23.4 % (normal 15.4 to 48.5)

[redacted] **20[redacted] LYMPHOCYTES %:** 0.082 % (normal 0.2 to 0.4)

[redacted] **20[redacted] LYMPHOCYTES %:** 10.9 % (normal 15.4 to 48.5)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.460 X10**9/L (normal0.8 to 4)

[redacted] **20[redacted] MCV:** 106 FL (normal 79 to 96)

[redacted] **20[redacted] MCV:** 105 FL (normal 79 to 96)

[redacted] 20[redacted] MEAN CORPUSTULAR HEMOGLOBIN: 33.800 PG (normal 27 to 31)

[redacted] **20[redacted] MONOCYTES:** 0.24 G/L (normal 0.12 to 0.92)

[redacted] **20[redacted] MONOCYTES:** 0.75 X10**3/MCL (normal 0.12 to 0.92)

[redacted] **20[redacted] MONOCYTES %:** 5 % (normal 2.6 to 10.1)

[redacted] **20[redacted] MONOCYTES %:** 0.007 % (normal 0.03 to 0.1)

[redacted] **20[redacted] MONOCYTES %:** 8.6 % (normal 2.6 to 10.1)

[redacted] **20[redacted] NEUTROPHILS:** 6.9 X10**3/MCL (normal 1.96 to 7.23)

[redacted] **20[redacted] NEUTROPHILS %:** 70 % (normal 40.5 to 75)

[redacted] **20[redacted] NEUTROPHILS %:** 0.907 % (normal 0.5 to 0.75)

[redacted] **20[redacted] NEUTROPHILS %:** 80.1 % (normal 40.5 to 75.0)

[redacted] **20[redacted] NEUTROPHILS ABS:** 5.070 X10**9/L (normal 2 to 7.5)

[redacted] 20[redacted] OCCULT BLOOD STOOL: Weak positive

[redacted] **20[redacted] PHOSPHORUS:** 1.01 MMOL/L (normal 0.71 to 1.65)

[redacted] **20[redacted] PHOSPHORUS:** 1.26 MMOL/L (normal 0.71 to 1.65)

[redacted] **20[redacted] PLATELETS:** 239 G/L (normal 140 to 400)

[redacted] **20[redacted] PLATELETS:** 162 X10**3/MCL (normal 140 to 400)

[redacted] **20[redacted] POTASSIUM:** 0.61 MMOL/L (normal 0.83 to 1.96)

[redacted] **20[redacted] PREALBUMIN:** 0.19 G/L (normal 0.2 to 0.4)

[redacted] **20[redacted] PT:** 14.6 SEC (normal 9.4 to 12.5)

[redacted] 20[redacted] R-GLUTAMYL TRANSPEPTIDASE: 106.90 U/L (normal 0 to 60)

[redacted] **20[redacted] RBC:** 3.9 TI/L (normal 4.5 to 6.4)

[redacted] **20[redacted] RBC:** 4.6 X10**6/MCL (normal 4.5 to 6.4)

[redacted] 20[redacted] RESISTANCE TO GP210 ANTIBODY: Negative

[redacted] 20[redacted] RESISTANCE TO SP100 ANTIBODY: Negative

[redacted] 20[redacted] RETINOL BINDING PROTEIN: 18.70 MG/L (normal 25 to 70)

[redacted] 20[redacted] RO-52 ANTIBODIES: Negative

[redacted] **20[redacted] SERUM BICARBONATE:** 22.3 MMOL/L (normal 17.0 to 30.6)

[redacted] **20[redacted] SERUM CHLORIDE:** 101 MMOL/L (normal 94 to 112)

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

[redacted] **20[redacted] SERUM POTASSIUM:** 3.9 MMOL/L (normal 3.5 to 5.2)

[redacted] **20[redacted] SERUM SODIUM:** 138 MMOL/L (normal 132 to 147)

[redacted] **20[redacted] TOTAL BILE ACID:** 17.74 umol/L (normal 0 to 10)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 19 umol/L (normal 3 to 21)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 18 umol/L (normal 3 to 21)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 44.64 umol/L (normal 5 to 21)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 46.19 umol/L (normal 5 to 21)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 37.18 umol/L (normal 5 to 21)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 27 umol/L (normal 3 to 21)

[redacted] **20[redacted] TOTAL IGE:** 55.50 kua/l (normal 0 to 60)

[redacted] **20[redacted] TOTAL PROTEIN:** 66 G/L (normal 61 to 84)

[redacted] **20[redacted] TRIGLYCERIDES:** 1.58 MMOL/L (normal 0.56 to 3.62)

[redacted] **20[redacted] TRIGLYCERIDES (GPO):** 2.23 MMOL/L (normal 0.56 to 3.62)

[redacted] **20[redacted] UREA NITROGEN:** 6.2 MMOL/L (normal 1.4 to 8.6)

[redacted] 20[redacted] URINE BACTERIA: Present

[redacted] 20[redacted] URINE LIQUID SILK: Positive

[redacted] 20[redacted] URINE MICRO PANEL: Positive

[redacted] 20[redacted] URINE TEST: MUCOUS-Present

[redacted] 20[redacted] URINE UROBILINOGEN: 1 + (normal 1.005 to 1.03)

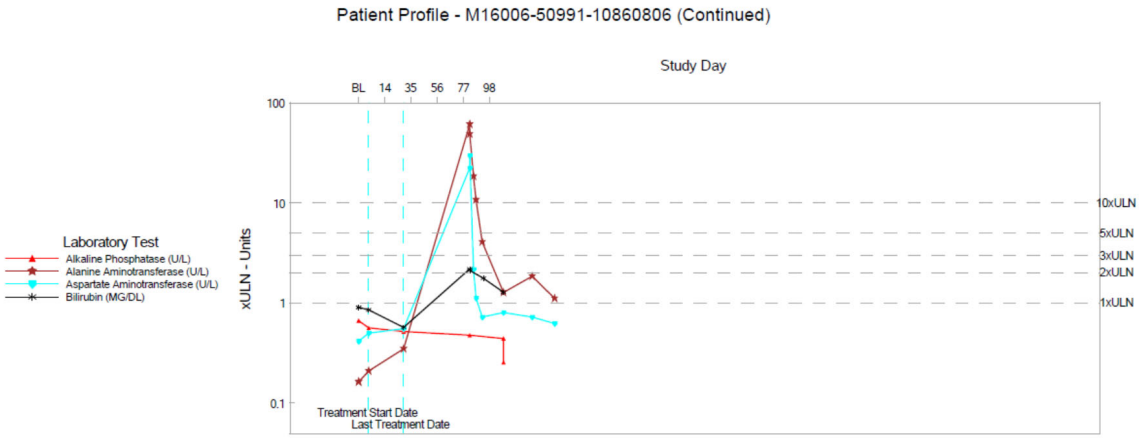
[redacted] **20[redacted] WBC:** 4.74 GI/L (normal 3.80 to 10.70)

[redacted] **20[redacted] WBC:** 5.590 X10**9/L (normal 4 to 10)

[redacted] **20[redacted] WBC:** 8.62 X10**3/MCL (normal 3.80 to 10.70)

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

ALT ([redacted]20[redacted] / Day -20) 7 U/L (reference range: 6-34 U/L), AST ([redacted]20[redacted] / Day -20) 15 U/L (reference range: 11-36 U/L), Bilirubin ([redacted]20[redacted] / Day -20) 19 umol/L (reference range: 3-21 umol/L) ALT ([redacted]20[redacted] / Day 1) 9 U/L (reference range: 6-34 U/L), AST ([redacted]20[redacted] / Day 1) 18 U/L (reference range: 11-36 U/L), Bilirubin ([redacted]20[redacted] / Day 1) 18 umol/L (reference range: 3-21 umol/L) ALT ([redacted]20[redacted] / Day 82) 2155 U/L (reference range: 3-35 U/L), AST ([redacted]20[redacted] / Day 82) 1198 U/L (reference range: 15-40 U/L), Bilirubin ([redacted]20[redacted] / Day 82) 46.19 umol/L (reference range: 5-21 umol/L) ALT ([redacted]20[redacted] / Day 92) 143 U/L (reference range: 3-35 U/L), AST ([redacted]20[redacted] / Day 92) 29 U/L (reference range: 15-40 U/L), Bilirubin ([redacted]20[redacted] / Day 93) 37.18 umol/L (reference range: 5-21 umol/L) ALT ([redacted]20[redacted] / Day 109) 55 U/L (reference range: 6-43 U/L), AST ([redacted]20[redacted] / Day 109) 29 U/L (reference range: 11-36 U/L), Bilirubin ([redacted]20[redacted] / Day 109) 27 umol/L (reference range: 3-21 umol/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
扁桃炎	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	3[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: DIFFUSE FATTY LIVER DISEASE	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: INTESTINAL FISTULA BETWEEN	20[redacted]
CHOLELITHIASIS: GALLSTONE	20[redacted]
OTHER: ANAL FISTULA	20[redacted]
OTHER: CHRONIC GASTRITIS	20[redacted]
OTHER: DUODENITIS	20[redacted]
OTHER: INFLAMMATION OF THE LEFT LOWER LOBE	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 32	32

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]

INFLIXIMAB	400 mg	OTHER: WEEK3?WEEK9	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: Q8W	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: Q4W	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: Q8W	Y-M: 20[redacted]
INFLIXIMAB	500 mg	OTHER: Q4W	Y-M: 20[redacted]
OTHER NUTRIENTS	2000 mL	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	OTHER: QW	Y-M: 20[redacted]
BLINDED THERAPY	120 mg	OTHER: Q2W	Y-M: 20[redacted]
METHYLPREDNISOLONE	48 mg	QD	Y-M: 20[redacted]
THALIDOMIDE	150 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	500 mg	OTHER: Q6W	Y-M: 20[redacted]
ADALIMUMAB	80 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	500 mg	OTHER: Q4W	Y-M: 20[redacted]
INFLIXIMAB	500 mg	OTHER: Q6W	Y-M: 20[redacted]
INFLIXIMAB	500 mg	OTHER: Q4W	Y-M: 20[redacted]
COLOPEG	180 g	QD	Y-M: 20[redacted] / -29
PROPOFOL	UNKNOWN mL	QD	Y-M: 20[redacted] / -29
COLOPEG	205.68 g	QD	Y-M: 20[redacted] / -8
PROPOFOL	UNKNOWN mL	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
BCG Vaccine	Not reported.	Not reported.	Not reported.	Not reported.
DEXAMETHASONE	10 mg	OTHER: ACCORDING TO THE NEED TO USE	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 57
IBUPROFEN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 57
PIPERACILLIN W/SULBACTAM	UNKNOWN mL	OTHER: ACCORDING TO THE NEED TO USE	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 57
ALANYL GLUTAMINE	50 mL	QD	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 63
SOLUTIONS FOR PARENTERAL NUTRITION	250 mL	QD	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 63
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 64
SULPERAZON	3 g	OTHER: Q12H	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 64
VERAMID	2 mL	QD	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 59

GLUTATHIONE	0.4 g	TID	Y-M: 20[redacted]-[redacted] / 59	Y-M: 20[redacted]-[redacted] / 81
MANNITOL	250 mL	QD	Y-M: 20[redacted]-[redacted] / 60	Y-M: 20[redacted]-[redacted] / 60
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted]-[redacted] / 63	Y-M: 20[redacted]-[redacted] / 63
OTHER NUTRIENTS	2000 mL	QD	Y-M: 20[redacted]-[redacted] / 63	Y-M: 20[redacted]-[redacted] / 155
CEFIXIME	50 mg	BID	Y-M: 20[redacted]-[redacted] / 64	Y-M: 20[redacted]-[redacted] / 81

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

Event Description ACUTE PURULENT TONSILLITIS

Preferred term 扁桃炎

AE Onset Date / Rx Day [redacted]20[redacted] / 54 (22 DAYS AFTER LAST TREATMENT)

Age at AE Onset 3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 55): Leukocytes: 9.34 [3.5 - 9.5] 10^9/L; Lymphocytes: 0.37 [0.8 - 4.5] 10^9/L; NPTST060-CK: 302 [10 - 190] U/L; NPTST070-CRP: 73.33 [0 - 10] mg/L; NPTST078-D-DIMER: 5570 [0 - 550] ng/mL; NPTST096-FBG: 4.27 [2 - 4] g/L; NPTST097-FDP: 15.2 [0 - 5] Unit not reported; NPTST115-GGT: 147 [0 - 49] U/L; Neutrophils: 8.8 [2 - 7] 10^9/L; [redacted]20[redacted] (Rx Day 58): Alanine Aminotransferase: 48.18 [0 - 40] U/L; Albumin: 30.51 [40 - 55] g/L; Aspartate Aminotransferase: 48.34 [0 - 40] U/L; Bilirubin: 14.14 [5 - 21] umol/L; C Reactive Protein: 71.83 [0 - 3] mg/L; Erythrocytes: 3.960 [4 - 5.5] 10^12/L; Glucose: 6.13 [3.89 - 6.11] mmol/L; Hematocrit: 0.345 [0.35 - 0.45] L/L; Hemoglobin: 116.000 [120 - 160] g/L; Leukocytes: 7.410 [4 - 10] 10^9/L; Lymphocytes/Leukocytes: 0.192 [0.2 - 0.4] Unit not reported; Monocytes: 1.310 [0 - 1] 10^9/L; Monocytes/Leukocytes: 0.177 [0.03 - 0.1] Unit not reported; NPTST002-A/G: 0.52 [1.2 - 2.4] Unit not reported; NPTST022-APOA1: 0.66 [1.09 - 2.28] g/L; NPTST046-BUN: 9.59 [2.8 - 7.1] mmol/L; NPTST069-CO2CP: 21.86 [22 - 29] mmol/L; NPTST074-CYS-C: 1.76 [0 - 1.02] mg/L; NPTST076-D DIMER QUANTIFICATION: 1.04 [0 - 0.5] Unit not reported; NPTST079-DBIL: 4.84 [0 - 3.4] umol/L; NPTST091-ESR: 99 [0 - 15] mm/h; NPTST117-GLB: 58.46 [20 - 40] g/L; NPTST130-HDL-C: 0.76 [0.78 - 2.2] mmol/L; NPTST141-IBIL: 9.30 [5 - 17.6] umol/L; NPTST157-LP(A): 531.7 [0 - 300] mg/L; NPTST186-PA: 0.13 [0.2 - 0.4] g/L; NPTST193-PCT: 6.960 [0 - 0.5] ng/mL; NPTST211-R-GT: 226.18 [0 - 60] U/L; NPTST214-RBP: 20.80 [25 - 70] mg/L; NPTST257-TBA: 13.46 [0 - 10] umol/L; NPTST262-TP: 88.97 [65 - 85] g/L

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 51): CHEST SCAN +3D: MICROPROLIFERATION IN THE ANTERIOR BASAL SEGMENT OF THE UPPER LOBE AND LOWER LOBE OF THE RIGHT LUNG;　A LITTLE INFLAMMATION IN BOTH LOWER LUNGS; COLOR ULTRASOUND: SEGMENTAL THICKENING AND RICH BLOOD SUPPLY OF SMALL INTESTINE, ILEUM AND SIGMOID COLON WERE CONSIDERED IN GROUPS 4-6.　SIX GROUPS OF SMALL INTESTINAL-TERMINAL ILEUM INTERINTESTINAL FISTULAS; CT- TOTAL ABDOMINAL PLAIN SCAN + ENHANCEMENT: 1. FATTY LIVER, SLIGHTLY LOW-DENSITY ENHANCED LESION IN THE RIGHT ANTERIOR LOBE OF THE LIVER;　2. CHOLECYSTOLITHIASIS WITH CHOLECYSTITIS;　LEFT RENAL CYST; 3.　4. LOCAL THICKENING OF THE INTESTINAL WALL IN THE RIGHT ILIAC FOSSA REGION ACCOMPANIED BY INFLAMMATORY EXUDATION

AE Stopped Rx Day 64 (32 DAYS AFTER LAST TREATMENT)

Duration of AE 11 DAYS

Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INTESTINAL FISTULA CANNOT BE RULED OUT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:20:26
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

中国の治験責任医師からの報告。本被験者は3[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，急性化膿性扁桃炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，びまん性脂肪肝疾患，腸管瘻，痔瘻，十二指腸炎，左肺下葉の炎症，非喫煙者及び非飲酒者であった。

投与 54 日後，被験者は急性化膿性扁桃炎を発現した。投与 64 日後，急性化膿性扁桃炎は消失した。

投与 54 日後の午後，被験者は最高 40.6°C の発熱の急性発現及び冷感があった。同日の後程，被験者は病院を受診し，入院した。臨床検査及び画像検査が行われた。全腹部 CT が行われ，右腸骨窩に末梢性炎症性滲出を伴う限局性腸壁肥厚が認められた。急性化膿性扁桃炎及びクローン病の両方が包括的に検討された。ピペラシリン／スルバクタム，デキサメタゾン及びイブプロフェンによる治療が開始されたが，発熱の再発は消失しなかった。投与 57 日後，被験者の発熱の最高値は 40.3°C であった。投与 58 日後，追加の診断及び治療のため被験者は別の病院に転院した。入院後，臨床検査，胸部CT検査，腹部超音波検査などの精密検査が完了した。胸部CT検査の結果，右肺の上葉及び下葉の前肺底区に微増殖及び両下肺にわずかな炎症が認められた。腹部超音波検査の結果，部分的肥厚及び小腸の豊富な血液供給を伴う小型の腸管内瘻が回腸末端に認められた。被験者のクローン病は「はっきりしており」，抗感染症治療後は発熱が認められなかった。投与 64 日後，被験者は退院した。

投与された薬剤は，デキサメタゾンリン酸エステルナトリウム，セフォペラゾン／スルバクタム，セフィキシム，ランソプラゾール，alanyl glutamine，脂肪乳剤及びアミノ酸（18），

aminophenazone/barbital sodium，塩酸メトクロプラミド，経腸栄養懸濁液（TPF），ピペラシリン／スルバクタム，デキサメタゾン及びイブプロフェンであった。

The patient’s past medications include:

AZATHIOPRINE for CROHN'S DISEASE ([redacted])

PREDNISONE ACETATE for CROHN'S DISEASE ([redacted])

INFLIXIMAB for CROHN'S DISEASE ([redacted])

METHOTREXATE for CROHN'S DISEASE ([redacted])

MEDROL for CROHN'S DISEASE ([redacted])

THALIDOMIDE for CROHN'S DISEASE ([redacted])

ADALIMUMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Acute tonsillitis (10001093) (Tonsillitis (10044008)) [v.23.0] [10001093]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of ACUTE PURULENT TONSILLITIS

- **Investigator:** Intestinal fistula cannot be ruled out

- **AbbVie:** Tonsillitis is a common event worldwide and is generally the result of a common viral or bacterial infection.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL CT SCAN:** 1. Fatty liver, slightly low-density enhanced lesion in the right anterior lobe of the liver; 2. Cholecystolithiasis with cholecystitis; Left renal cyst; 3. Local thickening of the intestinal wall in the right iliac fossa region accompanied by inflammatory exudation

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Segmental thickening and rich blood supply of small intestine, ileum and sigmoid colon were considered in groups 4-6. Six groups of small intestinal-terminal ileum interintestinal fistulas.

[redacted] 20[redacted] ALANINE AMINOTRANSFERASE: 48.18 U/L (normal 0 to 40)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 48.34 U/L (normal 0 to 40)

[redacted] **20[redacted] BILIRUBIN:** 4.84 umol/L (normal 0 to 3.4)

[redacted] **20[redacted] BODY TEMPERATURE:** Highest 40.6 degrees Celsius

[redacted] **20[redacted] BODY TEMPERATURE:** Highest 40.3 degrees Celsius

[redacted] **20[redacted] BUN:** 9.59 MMOL/L (normal 2.80 to 7.10)

[redacted] **20[redacted] CHEST CT SCAN:** Micro proliferation in the anterior basal segment of the upper lobe and lower lobe of the right lung; a little inflammation in both lower lungs

[redacted] **20[redacted] CK:** 302 U/L (normal 10 to 190)

[redacted] **20[redacted] CRP:** 73.33 mg/L (normal 0 to 10)

[redacted] **20[redacted] CRP:** 71.83 MG/L (normal 0 to 3)

[redacted] **20[redacted] D-DIMER:** 5570 PG/ML (normal 0 to 550)

[redacted] **20[redacted] D-DIMER:** 1.04 MG/ML (normal 0 to 0.5)

[redacted] **20[redacted] ESR:** 99 mm/h (normal 0 to 15)

[redacted] **20[redacted] FDP:** 15.2 ug/mL (normal 0 to 5)

[redacted] **20[redacted] GGT:** 147 U/L (normal 0 to 49)

[redacted] **20[redacted] GGT:** 226.18 U/L (normal 0 to 60)

[redacted] **20[redacted] GLOBULIN:** 58.46 G/L (normal 20 to 40)

[redacted] **20[redacted] LIPOPROTEIN (A):** 531.7 MG/L (normal 0 to 300)

[redacted] **20[redacted] NEUTROPHILS ABS:** 8.8 X10**9/L (normal 2.0 to 7.0)

[redacted] 20[redacted] NUCLEIC ACID TESTING FOR COVID-19: Negative

[redacted] 20[redacted] PLATELET COUNT: 178 X10**9/L

[redacted] **20[redacted] PROCALCITONIN:** 6.960 NG/ML (normal 0 to 0.5)

[redacted] **20[redacted] TOTAL BILE ACIDS:** 13.46 umol/L (normal 0 to 10)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9.34 X10**9/L (normal 3.5 to 9.5)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.410 X10**9/L (normal 4.0 to 10.0)

M16-000 試験 Sub-study 1

治験の標題： A Multicenter, Randomized, Double-Blind, Placebo Controlled 52-Week Maintenance and an Open-Label Extension Study of the Efficacy and Safety of Risankizumab in Subjects with Crohn's Disease	
施設数 / 実施国名： Sub-study 1（以下「SS1」）：273 施設 / 44 ヵ国（アルゼンチン，オーストラリア，オーストリア，ベラルーシ，ベルギー，ボスニア・ヘルツェゴヴィナ，ブルガリア，カナダ，チリ，中国，コロンビア，クロアチア，チェコ共和国，デンマーク，エジプト，エストニア，フランス，ドイツ，ギリシャ，アイルランド，イスラエル，イタリア，日本，マレーシア，メキシコ，オランダ，ニュージーランド，ノルウェー，ポーランド，ポルトガル，ルーマニア，ロシア，セルビア，シンガポール，スロバキア，南アフリカ，韓国，スペイン，スウェーデン，スイス，台湾，ウクライナ，イギリス，米国）	
治験責任医師： [redacted], MD, PhD，他	
公表文献 (参考資料) ： なし	
治験期間： 最初の被験者の初回来院日：2018 年 4 月 9 日 データカットオフ日：20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ：III
治験の種類： SS1：多施設共同，ランダム化，二重盲検，プラセボ対照，維持療法	
目的： SS1：導入療法試験（M16-006 試験又は M15-991 試験）のリサンキズマブ静脈内（以下「IV」）投与の導入療法により臨床的改善を達成した，導入療法試験のベースラインの Simple Endoscopic Score for Crohn's Disease（以下「SES-CD」）が 6 以上（病変が回腸に限局している場合は 4 以上）の中等症から重症の活動性クローン病患者を対象として，維持療法におけるリサンキズマブの有効性及び安全性を，リサンキズマブを休薬した患者と比較して評価する。 本項では，SS1 の治験総括報告書より投与 52 週時までの有効性及び安全性データを記述する。最後の被験者の投与 52 週時 Visit の完了は 20[redacted] 年 [redacted] 月 [redacted] 日であった。	
被験者数 (計画時と解析時) ： 計画時：1250 例（M16-000 試験全体） 解析時：712 例（SS1）	
診断と主要な組入れ基準： 導入療法試験に組み入れられ，試験を完了した被験者を対象とした。導入療法試験の最終 Visit に，導入療法試験のベースラインと比較して臨床的改善（平均 1 日排便回数［以下「SF」］が 30%以上減少及び / 又は平均 1 日腹痛［以下「AP」］スコアが 30%以上減少，かついずれもベースラインより悪化していない）を達成している必要があった。	
治験方法： 本試験は，導入療法試験に組み入れられ，導入療法試験の最終 Visit に臨床的改善を達成した被験者を対象とした，第 III 相，多施設共同試験であった。 本試験は 3 つの Sub-study で構成された。SS1 は 52 週間のランダム化，二重盲検，プラセボ対照維持療法試験であった。Sub-study 2（以下「SS2」）は 52 週間のランダム化，探索的維持療法試験であり，2 種類の投与レジメン（治療薬物モニタリング［TDM］と用量漸増に対する臨床評価［CA］）を評価する。Sub-study 3（以下	

「SS3」）は非盲検，長期継続投与試験である。本項では，SS1 の結果のみを記述する。

SS1 は最大約 68 週間であり，52 週間の維持療法期，及び治験薬の最終投与から 140 日間の追跡調査期（ただし，SS3 に継続参加する被験者は除く）からなる。

SS1 では，生物学的製剤による前治療で効果不十分又は不耐容であった被験者（以下「Bio-IR」）及び / 又は Bio-IR 以外の被験者で，従来の治療に対して効果不十分又は不耐容の被験者（過去に生物学的製剤による治療を受けたが，効果不十分又は不耐容以外の理由で投与を中止した被験者を含む）（以下「non Bio-IR」）を対象とした。

SS1 はランダム化された部分とランダム化されなかった部分で構成した。ランダム化された部分は主要な試験であった。導入療法試験の投与 12 週時又は導入療法期 2 の投与 24 週時にリサンキズマブ IV 投与の導入療法で臨床的改善を達成し，導入療法試験のベースラインの SES-CD が 6 以上（病変が回腸に限局している場合は 4 以上）であった被験者を，リサンキズマブ 180 mg 皮下（以下「SC」）投与 8 週毎（以下「Q8W」）若しくは 360 mg SC 投与 Q8W でのリサンキズマブの継続投与，又はリサンキズマブの休薬（盲検性維持のため，プラセボ SC 投与 Q8W）（以下「休薬群［プラセボ群］」）のいずれかに 1:1:1 の比で再ランダム化した。

SS1 のランダム化されなかった部分には，導入療法試験のプラセボ IV 投与にて臨床的改善を達成した被験者及びリサンキズマブ SC 投与で導入療法試験終了時に臨床的改善を達成した被験者を組み入れた。これらの被験者は盲検下で同じ治験薬を継続投与する群（プラセボ SC 投与又はリサンキズマブ SC 投与のいずれか）に割り付け，有効性の主解析からは除外した。

SS1 で効果不十分となった被験者は，症状の活動性が増加し，客観的炎症マーカーによって確認された場合，投与 16 週時以降，非盲検下でリサンキズマブのレスキュー治療を受けた。

有効性解析では，SS1 に組み入れられた被験者のベースラインは，導入療法試験のベースライン Visit を用いた。安全性解析については，導入療法試験でリサンキズマブを投与された被験者のベースラインは，導入療法試験でのリサンキズマブ初回投与前の最終測定と定義した。その他の被験者のベースラインは，導入療法試験での治験薬初回投与前の最終測定と定義した。投与 0 週時は，SS1 の初回 Visit と定義した。導入療法試験の最終 Visit（投与 12 週時又は投与 24 週時）を SS1 の投与 0 週時 Visit とみなした。

被験薬，用量，投与方法及びバッチ番号：

SS1 では，盲検下でリサンキズマブ 180 mg 又は 360 mg を投与 0，8，16，24，32，40 及び 48 週時に SC 投与した。

レスキュー治療は非盲検下でリサンキズマブ 1200 mg を単回 IV 投与し，その後非盲検下でリサンキズマブ 360 mg を Q8W で SC 投与した。リサンキズマブのレスキュー治療は，投与 16 週時 Visit 以降いつでも投与可能とした（レスキュー治療 Visit は最大 2 回までとした）。

リサンキズマブは，90 mg/mL の溶液として注入用バイアル（バッチ番号：[redacted]）及び 90 mg/mL の注射用プレフィルドシリンジ（バッチ番号：[redacted]）として提供された。

治療期間：

SS1 及び SS2：52 週間の維持療法期及び 140 日間の追跡調査期

SS3：最大 220 週間，又は治験中止まで

対照薬，用量，投与方法及びバッチ番号：

盲検下でプラセボを投与 0，8，16，24，32，40 及び 48 週時に SC 投与した。

プラセボは，注入用バイアル（バッチ番号：[redacted]）及び注射用プレフィルドシリンジ（バッチ番号：[redacted]）として提供された。

評価基準：

有効性：

米国以外における主要評価項目（co-primary endpoints）は，以下とした。

・投与 52 週時の臨床的寛解*を達成した被験者の割合

・投与 52 週時の内視鏡的改善**を達成した被験者の割合

米国における主要評価項目（co-primary endpoints）は，以下とした。

・投与 52 週時のクローン病活動度指数（以下「CDAI」）に基づく臨床的寛解（以下「臨床的 CDAI 寛解」）***を達成した被験者の割合

・投与 52 週時の内視鏡的改善を達成した被験者の割合

米国以外における副次評価項目は，以下とした。

1. 投与 52 週時の臨床的 CDAI 寛解を達成した被験者の割合
2. 投与 0 週時に臨床的寛解を達成していた被験者を対象とした投与 52 週時の臨床的寛解の維持を達成した被験者の割合
3. 投与 52 週時の内視鏡的治癒（潰瘍が治癒した状態）を達成した被験者の割合
4. 投与 52 週時の内視鏡的寛解を達成した被験者の割合
5. 投与 52 週時の炎症性腸疾患質問票（以下「IBDQ」）トータルスコアの導入療法試験のベースラインからの平均変化量
6. 投与 52 週時の慢性疾患治療-疲労の機能評価（以下「FACIT-F」）の導入療法試験のベースラインからの平均変化量
7. 導入療法試験のベースライン時にステロイドを使用していた被験者を対象とした投与 52 週時の臨床的寛解（コルチコステロイド非使用）を達成した被験者の割合
8. 投与 52 週時の CDAI に基づく臨床的改善（以下「臨床的 CDAI 改善」）を達成した被験者の割合
9. 投与 52 週時の臨床的寛解かつ内視鏡的改善を達成した被験者の割合
10. 投与 52 週時の高度臨床的改善を達成した被験者の割合
11. 投与 52 週時の臨床的寛解かつ内視鏡的寛解を達成した被験者の割合
12. 投与 0 週時から投与 52 週時までの曝露期間で調整したクローン病関連で入院した被験者の割合
13. 投与 52 週時の SF-36 健康調査票（以下「SF-36」）身体的側面の（以下「QoL」）サマリー（PCS）スコアの導入療法試験のベースラインからの変化量

米国における副次評価項目は，以下とした。

1. 投与 52 週時の臨床的寛解を達成した被験者の割合
2. 投与 0 週時に臨床的 CDAI 寛解を達成していた被験者を対象とした投与 52 週時の臨床的 CDAI 寛解の維持を達成した被験者の割合
3. 投与 52 週時の内視鏡的治癒（潰瘍が治癒した状態）を達成した被験者の割合
4. 投与 52 週時の内視鏡的寛解を達成した被験者の割合
5. 投与 52 週時の FACIT-F の導入療法試験のベースラインからの変化量
6. 導入療法試験のベースライン時にステロイドを使用していた被験者を対象とした投与 52 週時の臨床的 CDAI 寛解（コルチコステロイド非使用）を達成した被験者の割合
7. 投与 52 週時の臨床的 CDAI 改善を達成した被験者の割合
8. 投与 52 週時の SF 寛解を達成した被験者の割合
9. 投与 52 週時の AP 寛解を達成した被験者の割合
10. 投与 52 週時の臨床的 CDAI 寛解かつ内視鏡的改善を達成した被験者の割合
11. 投与 52 週時の完全寛解（臨床的 CDAI 寛解かつ内視鏡的寛解）を達成した被験者の割合
12. 投与 0 週時から投与 52 週時までの曝露期間で調整したクローン病関連で入院した被験者の割合

* 臨床的寛解：平均 1 日 SF が 2.8 回以下でベースラインより悪化していない，かつ平均 1 日 AP スコアが 1 以下でベースラインより悪化していない

** 内視鏡的改善：中央判定の評価者によるスコア判定で SES-CD がベースラインから 50%超減少（病変が回腸に限局している被験者でベースラインの SES-CD が 4 の場合，ベースラインからの減少が 2 以上）

*** 臨床的 CDAI 寛解：CDAI スコアが 150 未満

薬物動態及び免疫原性：
血清中リサンキズマブ濃度，リサンキズマブに対する抗薬物抗体及び中和抗体を測定した。

安全性：
試験期間を通して，有害事象，バイタルサイン，心電図，身体検査，臨床検査値，及び製品品質苦情を評価した。

統計手法：

有効性：

有効性の主要評価項目について，本試験の投与 0 週時の臨床的寛解の達成状況及び本試験の投与 0 週時の内視鏡的改善（中央判定による）の達成状況，並びにリサンキズマブの導入療法試験の用量で調整した Cochran-Mantel-Haenszel（以下「CMH」）検定を用いて，リサンキズマブ各群とプラセボ群を比較した。主要評価項目（co-primary endpoints）及び副次評価項目について，多重性の検定手順を用いて，リサンキズマブ各群とプラセボ群との比較解析における第一種の過誤率を $\alpha = 0.05$（両側）に厳密に制御した。投与群間差の両側 95%信頼区間を CMH に基づき算出した。

連続変数で表される有効性の副次評価項目のうち，投与 0 週時 Visit 後の 1 時点でのみ収集すると規定された項目については，共分散分析（ANCOVA）モデルを用いて解析した。このモデルには，投与群，層別因子，並びに導入療法試験のベースライン及び投与 0 週時の各測定値を含めた。

主要解析は intent-to-treat（以下「ITT」）1A 解析対象集団を用いて実施した。ITT1A 解析対象集団は，治験薬を 1 回以上投与された被験者からなる ITT1 解析対象集団のランダム化された被験者のうち，導入療法試験でリサンキズマブ IV 投与を 12 週間のみ受けた，導入療法試験のベースラインの SES-CD が 6 以上（病変が回腸に限局している場合は 4 以上）の被験者とした。

薬物動態及び免疫原性：
各評価時点の血清中リサンキズマブ濃度を，投与群ごとに記述統計量を用いて要約した。抗薬物抗体の発現率をコホート別及び Visit 別に要約した。

安全性：
安全性は，安全性解析対象集団を用いて投与群間で比較した。SA1 解析対象集団は，SS1 で治験薬を 1 回以上投与されたすべての被験者とした。SA1A 解析対象集団は，SA1 解析対象集団のランダム化されたすべての被験者のうち，導入療法試験のベースラインの SES-CD が 6 以上（病変が回腸に限局している場合は 4 以上）であり，導入療法試験でリサンキズマブ IV 投与を 12 週間のみ受けた被験者とした。治験薬投与後に発現した有害事象は，発現被験者数及び割合別に要約した。臨床検査値の変動は，記述統計量で示し，分散分析（ANOVA）を用いて投与群間で比較した。バイタルサイン及び心電図パラメータも解析した。

内訳

SS1 では，542 例（リサンキズマブ 180 mg SC 群 179 例，360 mg SC 群 179 例，休薬群［プラセボ群］184 例）がランダム化され，治験薬を投与された。このうち，治験薬の投与を完了した被験者の割合は，リサンキズマブ 180 mg SC 群 91.6%，360 mg SC 群 89.4%，休薬群（プラセボ群）87.0%であり，投与群間でおおむね均衡していた。

170 例（リサンキズマブ 180 mg SC 群 31 例，360 mg SC 群 33 例，プラセボ群 106 例）はランダム化されず，先行試験と同じ治験薬を投与された。このうち，治験薬の投与を完了した被験

者の割合は，リサンキズマブ 360 mg SC 群で 180 mg SC 群及びプラセボ群と比較して高かった（リサンキズマブ 180 mg SC 群 83.9%，360 mg SC 群 100%，プラセボ群 77.4%）。

有効性の結果

ITT1A 解析対象集団において，米国の co-primary endpoints である臨床的 CDAI 寛解及び内視鏡的改善を達成した被験者の割合は，リサンキズマブ 180 mg SC 群（臨床的 CDAI 寛解 55.4%，内視鏡的改善 47.1%，以下同順）及び 360 mg SC 群（52.2%，46.5%）で休薬群（プラセボ群）（40.9%，22.0%）と比較して統計学的に有意に高く（いずれも各群で $P < 0.01$），いずれもが達成された。米国以外の co-primary endpoints である臨床的寛解及び内視鏡的改善を達成した被験者の割合は，リサンキズマブ 360 mg SC 群（臨床的寛解 51.8%，内視鏡的改善 46.5%，以下同順）で休薬群（プラセボ群）（39.6%，22.0%）と比較して統計学的に有意に高く（いずれも $P < 0.01$），いずれもが達成されたが，リサンキズマブ 180 mg SC 群（46.5%，47.1%）では co-primary endpoints は達成されなかった（臨床的寛解：$P = 0.124$，内視鏡的改善：$P < 0.001$）。

主要な部分集団である Bio-IR 部分集団及び non Bio-IR 部分集団において，co-primary endpoints の両評価項目の結果，全体として，ITT1A 解析対象集団の全体集団と同様の傾向が認められた。Non Bio-IR 部分集団で Bio-IR 部分集団と比較して概して有効性が高かった。導入療法試験の用量がリサンキズマブ 600 mg IV であった部分集団と 1200 mg IV 群であった部分集団で数値的に同様であったことから，導入療法試験の用量は，維持療法による投与 52 週時の有効性に影響を及ぼさなかったと考えられる。

米国以外の co-primary endpoints は，事前に規定した graphical testing procedure に基づき，リサンキズマブ 360 mg SC 群で休薬群（プラセボ群）と比較して統計学的に有意に高く，co-primary endpoints が達成されたが，リサンキズマブ 180 mg SC 群においては，co-primary endpoints が達成されなかったため，本評価項目で検定手順が終了となり，副次評価項目については統計学的に有意な差は認められなかった。米国の co-primary endpoints は，リサンキズマブ 180 mg SC 群及び 360 mg SC 群で休薬群（プラセボ群）と比較して統計学的に有意に高く，引き続き副次評価項目の検定手順を実施した。米国の副次評価項目について，リサンキズマブ 180 mg SC 群では，第 1 の副次評価項目の臨床的寛解で検定手順が終了となり，副次評価項目については統計学的に有意な差は認められなかった。リサンキズマブ 360 mg SC 群では，第 1 の副次評価項目の臨床的寛解について統計学的に有意であり，第 2 の副次評価項目の臨床的 CDAI 寛解の維持で検定手順が終了した。

内視鏡的寛解及び内視鏡的治癒（潰瘍が治癒した状態）の結果より，リサンキズマブ各群で休薬群（プラセボ群）と比較して臨床的に意義のある粘膜炎症の減少が認められた（いずれも，名目 P 値< 0.001）。臨床的寛解かつ内視鏡的改善，臨床的 CDAI 寛解かつ内視鏡的改善，臨床的寛解かつ内視鏡的寛解及び完全寛解の複合評価項目についても，リサンキズマブ各群と休薬群（プラセボ群）に投与群間差が認められた（いずれも，名目 P 値≤ 0.001）。全体として，これらの評価項目より，リサンキズマブ 360 mg SC 群の有効性は，180 mg SC 群と比較して，数値的に高く，明確な用量反応性が認められた。

投与 52 週時の臨床的 CDAI 寛解及び臨床的寛解の維持（投与 0 週時に臨床的寛解を達成していた被験者を対象とした投与 52 週時の臨床的寛解の維持）を達成した被験者の割合は，リサンキズマブ各群で休薬群（プラセボ群）と比較して，数値的に高かった（いずれも，名目 *P* 値 < 0.05）。

クローン病の徴候及び症状の評価項目について，投与 52 週時の臨床的 CDAI 改善，高度臨床的改善，SF 寛解及び AP 寛解を達成した被験者の割合は，リサンキズマブ各群で休薬群（プラセボ群）と比較して数値的に高かった（名目 *P* 値< 0.05［リサンキズマブ 180 mg SC 群の SF 寛解を除く］）。

ITT1A 解析対象集団のうち，約 30%の被験者が導入療法試験のベースラインにコルチコステロイドを使用していた。このうち，投与 52 週時の臨床的 CDAI 寛解（コルチコステロイド非使用）及び臨床的寛解（コルチコステロイド非使用）を達成した被験者の割合は，リサンキズマブ 180 mg SC 群で 360 mg SC 群及び休薬群（プラセボ群）と比較して高かった。

QoL 関連の評価項目である IBDQ，FACIT-F 及び SF-36 並びにクローン病関連の入院の発生については，全体として，すべての投与群間で数値的に同様であり，クローン病関連の入院はほとんど報告されなかった（各群で 5–9 例）。

全体として，その他の評価項目の結果は，co-primary endpoints 及び副次評価項目の結果を裏付けるものであった。

ITT1B 解析対象集団（リサンキズマブ 180 mg SC 群 14 例，360 mg SC 群 23 例，休薬群［プラセボ群］15 例）には，Low SES-CD（小腸大腸型病変又は大腸型病変の場合はベースラインの SES-CD が 3 以上 6 未満［病変が回腸に限局している場合は 3］）の被験者が含まれた。ITT1B 解析対象集団では，例数が少なかったため，その結果からは，有効性に関する明確な傾向は認められなかった。

ITT1C 解析対象集団は，2 つの集団，すなわち，導入療法試験にてリサンキズマブ 180 mg 又は 360 mg SC 投与により投与 24 週時に臨床的改善を達成した被験者，及び導入療法試験でプラセボ IV 投与により投与 12 週時に臨床的改善を達成した被験者から構成された。両被験者集団はいずれも，先行する導入療法試験で投与されていたものと同一の投与（リサンキズマブ 180 mg SC，360 mg SC 又はプラセボ）を受けた。リサンキズマブ SC 投与を引き続き受けた被験者では，全体として，主要解析対象集団（ITT1A 解析対象集団）でリサンキズマブ SC 投与を受けた被験者と数値的に同様の結果が認められた。導入療法試験でプラセボ IV 投与により臨床的改善を達成し，SS1 でプラセボ SC 投与を引き続き受けた被験者（プラセボ群 104 例）では，臨床的改善を達成した被験者の割合は 32.7%であった。また，プラセボ群では，投与 52 週時の臨床的 CDAI 寛解を達成した被験者の割合は 19.2%，臨床的寛解を達成した被験者の割合は 16.3%，内視鏡的改善を達成した被験者の割合は 13.5%であった。クローン病の徴候及び症状の評価項目について，プラセボ群（導入療法試験にてプラセボ IV 投与により臨床的改善を達成した被験者）での結果は，休薬群（プラセボ群）（ITT1A 解析対象集団のうち，導入療法試験にてリサンキズマブ IV 投与により臨床的改善を達成した被験者）と異なり，投与 52 週時の臨床的改善，臨床的寛解及び臨床的 CDAI 寛解を達成した被験者の割合は，休薬群（プラセボ群）で相対的に高

かった。この投与群間差はリサンキズマブの半減期に起因している可能性があり，ITT1A 解析対象集団の休薬群（プラセボ群）では，おおむね投与 16 週時まで導入療法に由来するリサンキズマブが残存していた。

ITT1D 解析対象集団は，リサンキズマブ IV の 12 週又は 24 週投与の導入療法により臨床的改善を達成した被験者のうち，導入療法試験のベースラインの SES-CD が 6 以上（病変が回腸に限局している場合は 4 以上）の被験者を含めた。ITT1D 解析対象集団の結果は，ITT1A 解析対象集団の結果と一致していた。

薬物動態及び免疫原性の結果

全体として，リサンキズマブ 180 mg 及び 360 mg を SC 投与したときの血清中リサンキズマブ濃度は，SS1 の維持療法期を通して経時的におおむね用量に比例した 2 倍の差がみられ，各投与群内での投与 16，32 及び 48 週時の投与前（トラフ）濃度が一定であったことから定常状態に達したことが示された。投与 52 週時の血清中リサンキズマブ濃度はその他の Visit と比較して高かったが，これは他の Visit では投与後 8 週間に検体を採取したのに対して，投与後 4 週間に採取したためであった。一方，休薬群（プラセボ群）では，リサンキズマブの血清中曝露量が測定可能であり（特に投与 16 週時），リサンキズマブの消失半減期が長いため，先行試験での IV 導入療法からのリサンキズマブがウォッシュアウトされるまでに長い時間がかかることが示された。更に，先行試験の導入療法（IV 投与又は SC 投与）にかかわらず，SS1 の規定 Visit の血清中リサンキズマブ濃度は，例数が限られていたリサンキズマブ 1200 mg IV の 24 週間投与の導入療法を受けた群を除いて，同じ維持療法用量ではおおむね同様であった。

ITT1A 解析対象集団のランダム化された被験者で，リサンキズマブ IV 投与の 12 週間の導入療法後に SC 投与の維持療法を受けた被験者では，リサンキズマブ全体として，治験薬投与に起因する抗薬物抗体の発現率（1.8%，4/224 例）及び中和抗体の発現率（0.4%，1/224 例）はいずれも低かった。抗薬物抗体及び中和抗体の発現率は，リサンキズマブ 180 mg SC 群（それぞれ 2.6%及び 0.9%）でリサンキズマブ 360 mg SC 群（それぞれ 0.9%及び 0%）と比較してわずかに高かった。同様に，24 週間の IV 投与の導入療法を受けた被験者又はランダム化されなかった被験者における抗薬物抗体の発現率（4.0%未満）及び中和抗体の発現率（0%）は低かった。リサンキズマブ IV 投与の 12 週間の導入療法の後，維持療法試験でリサンキズマブ投与に起因する抗薬物抗体が最初に認められるまでの期間は，リサンキズマブ 360 mg SC 群で 48.1 週間（1 例），180 mg SC 群で 15.6 週間から 48.3 週間であった。抗薬物抗体の抗体価は，SS1 の試験期間を通して 10–1540 であった。

安全性の結果

SA1 解析対象集団のランダム化された被験者のうち，1 件以上の有害事象を発現した被験者の割合は，リサンキズマブ 180 mg SC 群で 71.5%，360 mg SC 群で 72.1%であり，休薬群（プラセボ群）73.4%と同様であった。重篤な有害事象，高度の有害事象，及び治験薬の投与中止に至っ

た有害事象の発現割合は，リサンキズマブ 180 mg SC 群，360 mg SC 群及び休薬群（プラセボ群）で同様であった。死亡は認められなかった。リサンキズマブのレスキュー治療群の 2 例（1.3%）に重篤な有害事象の敗血症が認められたが，リサンキズマブ 180 mg SC 群，360 mg SC 群又は休薬群（プラセボ群）では重篤な敗血症は認められなかった。リサンキズマブ 180 mg SC 群，360 mg SC 群及び休薬群（プラセボ群）で発現割合が高かった有害事象は，クローン病（リサンキズマブ 180 mg SC 群 10.6%，360 mg SC 群 11.7%，休薬群［プラセボ群］17.4%，以下同順），上咽頭炎（9.5%，9.5%，13.6%），及び関節痛（8.4%，9.5%，10.9%）であった。有害事象のほとんどは，軽度又は中等度であった。特に注目すべき事象に分類された有害事象の発現割合は，おおむね投与群間で同程度であった。活動性結核，重篤な過敏症，及び委員会判定されたアナフィラキシー反応は認められなかった。主要心血管イベント（以下「MACE」）及び悪性腫瘍はまれであり，潜在的リスク因子を有する被験者に報告された。リサンキズマブ各群で認められた重篤な感染症の種類に，特定の傾向は認められなかった。重篤又は高度の肝関連事象は認められず，リサンキズマブ各群で認められた肝関連事象の基本語の大半は臨床検査値異常であった。投与群間の肝関連事象，臨床検査値及び外れ値の解析の包括的な評価から，肝障害に関する安全性の問題は認められなかった。過敏症の有害事象の発現割合は，リサンキズマブ 180 mg SC 群，360 mg SC 群及び休薬群（プラセボ群）で同様であった。重篤又は高度の注射部位反応，及び治験薬の投与中止に至った注射部位反応は認められなかった。注射部位反応はおおむね過敏症反応を示唆するものではなかった。有害事象，臨床検査，バイタルサイン又は心電図評価について，用量依存的な傾向は認められなかった。新たな安全性のリスクは特定されず，全体として安全性プロファイルは，リサンキズマブの既知の安全性プロファイルと一致していた。リサンキズマブのレスキュー治療を受けた被験者で，リサンキズマブ 180 mg SC 群，360 mg SC 群及び休薬群（プラセボ群）と比較して問題となる安全性の所見は認められなかった。

SA1 解析対象集団のランダム化されなかった被験者のうち，1 件以上の有害事象が報告された被験者の割合はリサンキズマブ 180 mg SC 群で 87.1%，360 mg SC 群で 78.8%，プラセボ SC 群で 77.4%であった。重篤な有害事象，高度の有害事象，及び治験薬の投与中止に至った有害事象の発現割合は，リサンキズマブ 180 mg SC 群，360 mg SC 群及びプラセボ群で同様であった。死亡は認められなかった。発現割合が高かった有害事象は，リサンキズマブ群全体では，クローン病（リサンキズマブ群全体 18.8%，180 mg SC 群 19.4%，360 mg SC 群 18.2%，以下同順），上咽頭炎（14.1%，9.7%，18.2%），腹痛（10.9%，16.1%，6.1%）及び関節痛（10.9%，9.7%，12.1%）であり，プラセボ群ではクローン病（29.2%），上咽頭炎（6.6%）及び腹痛（5.7%）であった。有害事象のほとんどは，軽度又は中等度であった。特に注目すべき事象に分類された有害事象の発現割合は，おおむね投与群間で同様であった。活動性結核，悪性腫瘍，重篤な過敏症，及び委員会判定されたアナフィラキシー反応は認められなかった。リサンキズマブ各群で，重篤な感染症が 1 例，非致死的な委員会判定された MACE が 1 例（2 件）報告された。投与群間の肝関連事象，臨床検査値及び外れ値の解析の包括的な評価から，肝障害に関する安全性の問題は認められなかった。過敏症の有害事象の発現割合は，リサンキズマブ 180 mg SC 群で 6.5%，360 mg SC 群で 6.1%，及びプラセボ群で 3.8%であった。重篤な注射部位反応，及び治

験薬の投与中止に至った注射部位反応は認められなかった。注射部位反応はおおむね過敏症反応を示唆するものではなかった。有害事象，臨床検査，バイタルサイン又は心電図評価について，用量依存的な傾向は認められなかった。新たな安全性のリスクは特定されず，全体として安全性プロファイルはリサンキズマブの既知の安全性プロファイルと一致していた。リサンキズマブのレスキュー治療を受けた被験者で，リサンキズマブ 180 mg SC 群，360 mg SC 群及びプラセボ群と比較して問題となる安全性の所見は認められなかった。

安全性解析の結果は，SA1 解析対象集団と SA1A 解析対象集団間で同様であった。

結論

維持療法試験（M16-000 試験 SS1）の結果は，リサンキズマブ SC 投与による維持療法を継続することを裏付けるものであった。米国の co-primary endpoints である臨床的 CDAI 寛解及び内視鏡的改善は，リサンキズマブ 180 mg SC 群及び 360 mg SC 群で達成された。米国以外の co-primary endpoints である臨床的寛解及び内視鏡的改善は，リサンキズマブ 360 mg SC 群で達成された。全体として，リサンキズマブ SC 投与を受けた被験者ではクローン病の徴候及び症状の評価項目を達成した被験者の割合が高かった。また，投与 52 週時の内視鏡的評価項目の結果から，リサンキズマブ各群で休薬群（プラセボ群）と比較して明確な効果が示された。更に，客観的な内視鏡的評価項目を達成した被験者の割合は経時的に増加し，リサンキズマブ各群では，炎症マーカーが更に減少した。一方，休薬群（プラセボ群）では，炎症マーカー及び SES-CD がいずれも経時的に増加し，客観的評価項目を達成した被験者の割合が経時的に減少した。クローン病の徴候及び症状の評価項目で認められた有効性は，リサンキズマブ 180 mg SC 群と 360 mg SC 群で同様であったが，より厳格な評価項目（内視鏡的寛解及び内視鏡的治癒［潰瘍が治癒した状態］）については，全体集団及び Bio-IR 集団で用量反応性が認められた。

導入療法試験にてリサンキズマブ 180 mg 又は 360 mg SC 投与により投与 24 週時に臨床的改善を達成した被験者（delayed response の被験者）で，12 週間のリサンキズマブ IV 投与の導入療法により臨床的改善を達成した被験者と同様の有効性が投与 52 週時に示されたことから，delayed response の被験者に対してもリサンキズマブ SC 投与の維持療法を継続することが裏付けられた。

中等症から重症の活動性クローン病患者に対してリサンキズマブ 180 mg SC 又は 360 mg SC 投与 Q8W を行ったとき，先行試験の導入療法にかかわらず，血清中リサンキズマブ濃度は 52 週間の維持療法期を通しておおむね用量比例関係が示された。リサンキズマブの消失半減期が長いため，休薬群（プラセボ群）では，先行試験における IV 投与の導入療法からのリサンキズマブの血清中曝露量の減少が測定できた。抗薬物抗体の陽性被験者数は限られていたが，リサンキズマブの曝露量に及ぼす免疫原性の明らかな影響は認められなかった。

維持療法としてのリサンキズマブの 1 年間投与は，おおむね安全で忍容性は良好であった。用量依存的なシグナルは認められなかった。新たな安全性のリスクは特定されず，全体として安全性プロファイルは，リサンキズマブの既知の安全性プロファイルと一致していた。

本試験の曝露状況の概要及び本試験で発現した有害事象を以下のとおり示す。

項目	ランダム化された被験者（SA1）	ランダム化されなかった被験者（SA1）
曝露状況の概要	表 1	表 2
有害事象の概要	-	表 3
すべての有害事象	表 4	表 5
治験薬と関連ありの有害事象	表 6	表 7
高度の有害事象	-	表 8
重篤な有害事象	-	表 9
中止に至った有害事象	-	表 10

表1

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RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-000 SUB-STUDY 1
R&D/21/0085 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.1__20.1

Extent of Exposure
Among Randomized Subjects
(SA1 Population)

		Risankizumab			
Exposure to study drug	Placebo SC [A] (N=184) n (%)	180 mg SC [A] (N=179) n (%)	360 mg SC [A] (N=179) n (%)	Total [A] (N=358) n (%)	Risankizumab Rescue Therapy [B] (N=150) n (%)
Duration interval (days)					
1 - 56	0	2 (1.1)	2 (1.1)	4 (1.1)	22 (14.7)
57 - 112	10 (5.4)	9 (5.0)	7 (3.9)	16 (4.5)	10 (6.7)
113 - 168	23 (12.5)	13 (7.3)	19 (10.6)	32 (8.9)	25 (16.7)
169 - 224	22 (12.0)	9 (5.0)	12 (6.7)	21 (5.9)	39 (26.0)
225 - 280	7 (3.8)	10 (5.6)	8 (4.5)	18 (5.0)	47 (31.3)
281 - 336	8 (4.3)	2 (1.1)	4 (2.2)	6 (1.7)	7 (4.7)
337 - 392	83 (45.1)	107 (59.8)	81 (45.3)	188 (52.5)	0
> 392	31 (16.8)	27 (15.1)	46 (25.7)	73 (20.4)	0
Duration (days)					
n	184	179	179	358	150
Mean (SD)	308.5 (109.30)	334.8 (101.50)	328.1 (106.59)	331.4 (103.98)	185.0 (80.92)
Median	385.5	389.0	390.0	390.0	202.5
Min, Max	105, 402	56, 423	56, 438	56, 438	8, 316

Note: SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
[A] Total exposure before receiving rescue therapy is defined as last dose date of study drug + 56 – first dose of date of study drug, or first dose date of study drug in the sub-study 3, if applicable – first dose date of study drug, or fist dose date of rescue therapy, if applicable – first dose date of study drug, whichever is shorter.
[B] Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. Total exposure for subjects after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. Total exposure after receiving rescue therapy is defined as last dose date of study drug + 56 – first dose of date of rescue therapy, or first dose date of study drug in the sub-study 3, if applicable – first dose date of rescue therapy, whichever is shorter.
Percentages calculated based on N in the header.

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表2

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RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-000 SUB-STUDY 1
R&D/21/0085 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.1__20.2

Extent of Exposure
Among Non-randomized Subjects
(SA1 Population)

		Risankizumab			
Exposure to study drug	Placebo SC [A] (N=106) n (%)	180 mg SC [A] (N=31) n (%)	360 mg SC [A] (N=33) n (%)	Total [A] (N=64) n (%)	Risankizumab Rescue Therapy [B] (N=61) n (%)
Duration interval (days)					
1 - 56	7 (6.6)	0	0	0	3 (4.9)
57 - 112	9 (8.5)	1 (3.2)	2 (6.1)	3 (4.7)	8 (13.1)
113 - 168	22 (20.8)	6 (19.4)	1 (3.0)	7 (10.9)	7 (11.5)
169 - 224	11 (10.4)	3 (9.7)	2 (6.1)	5 (7.8)	16 (26.2)
225 - 280	10 (9.4)	1 (3.2)	1 (3.0)	2 (3.1)	23 (37.7)
281 - 336	5 (4.7)	0	0	0	4 (6.6)
337 - 392	29 (27.4)	16 (51.6)	18 (54.5)	34 (53.1)	0
> 392	13 (12.3)	4 (12.9)	9 (27.3)	13 (20.3)	0
Duration (days)					
n	106	31	33	64	61
Mean (SD)	254.6 (125.48)	311.6 (113.85)	350.3 (95.52)	331.6 (105.76)	203.5 (69.38)
Median	251.5	389.0	391.0	390.0	217.0
Min, Max	56, 413	111, 425	105, 417	105, 425	14, 286

Note: SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
[A] Total exposure before receiving rescue therapy is defined as last dose date of study drug + 56 – first dose of date of study drug, or first dose date of study drug in the sub-study 3, if applicable – first dose date of study drug, or fist dose date of rescue therapy, if applicable – first dose date of study drug, whichever is shorter.
[B] Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. Total exposure for subjects after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. Total exposure after receiving rescue therapy is defined as last dose date of study drug + 56 – first dose of date of rescue therapy, or first dose date of study drug in the sub-study 3, if applicable – first dose date of rescue therapy, whichever is shorter.
Percentages calculated based on N in the header.

Program Source Code: [redacted]

表3

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RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-000 SUB-STUDY 1
R&D/21/0085 - CLINICAL/STATISTICAL

TABLE 14.3__1.2.1.7

Overview of Treatment-Emergent Adverse Events and All Deaths After Discontinuation of Study Treatment by Time Period
Among Non-randomized Subjects
(SA1 Population)

Time Period	Placebo SC (N=27) n (%)	Risankizumab 180 mg SC (N=5) n (%)	Risankizumab 360 mg SC (N=0) n (%)	Risankizumab Total (N=5) n (%)	Risankizumab Rescue Therapy* (N=9) n (%)
Last dose date +1 to 30 days after last dose date					
Subjects with any treatment-emergent					
Adverse event (AE)	7 (25.9)	1 (20.0)	0	1 (20.0)	2 (22.2)
AE related to COVID-19	0	0	0	0	0
AE related to study drug according to the investigator	2 (7.4)	1 (20.0)	0	1 (20.0)	0
Severe AE	1 (3.7)	0	0	0	0
Serious AE	2 (7.4)	0	0	0	0
AE leading to discontinuation of study drug	2 (7.4)	1 (20.0)	0	1 (20.0)	0
AE leading to death	0	0	0	0	0
All deaths					
Deaths occurring <= 140 days after last dose of study drug	0	0	0	0	0
Deaths occurring > 140 days after last dose of study drug	0	0	0	0	0
Deaths related to COVID-19	0	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

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TABLE 14.3__1.2.1.7

Overview of Treatment-Emergent Adverse Events and All Deaths After Discontinuation of Study Treatment by Time Period
Among Non-randomized Subjects
(SA1 Population)

Time Period	Placebo SC (N=27) n (%)	Risankizumab 180 mg SC (N=5) n (%)	Risankizumab 360 mg SC (N=0) n (%)	Risankizumab Total (N=5) n (%)	Risankizumab Rescue Therapy* (N=9) n (%)
31 days after last dose date to 60 days after last dose date					
Subjects with any treatment-emergent					
Adverse event (AE)	6 (22.2)	0	0	0	2 (22.2)
AE related to COVID-19	0	0	0	0	0
AE related to study drug according to the investigator	0	0	0	0	1 (11.1)
Severe AE	4 (14.8)	0	0	0	0
Serious AE	3 (11.1)	0	0	0	0
AE leading to discontinuation of study drug	2 (7.4)	0	0	0	0
AE leading to death	0	0	0	0	0
All deaths					
Deaths occurring <= 140 days after last dose of study drug	0	0	0	0	0
Deaths occurring > 140 days after last dose of study drug	0	0	0	0	0
Deaths related to COVID-19	0	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

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TABLE 14.3__1.2.1.7

Overview of Treatment-Emergent Adverse Events and All Deaths After Discontinuation of Study Treatment by Time Period
Among Non-randomized Subjects
(SA1 Population)

Time Period	Placebo SC (N=27) n (%)	Risankizumab 180 mg SC (N=5) n (%)	Risankizumab 360 mg SC (N=0) n (%)	Risankizumab Total (N=5) n (%)	Risankizumab Rescue Therapy* (N=9) n (%)
61 days after last dose date to 90 days after last dose date					
Subjects with any treatment-emergent					
Adverse event (AE)	3 (11.1)	0	0	0	0
AE related to COVID-19	0	0	0	0	0
AE related to study drug according to the investigator	0	0	0	0	0
Severe AE	1 (3.7)	0	0	0	0
Serious AE	2 (7.4)	0	0	0	0
AE leading to discontinuation of study drug	1 (3.7)	0	0	0	0
AE leading to death	0	0	0	0	0
All deaths					
Deaths occurring <= 140 days after last dose of study drug	0	0	0	0	0
Deaths occurring > 140 days after last dose of study drug	0	0	0	0	0
Deaths related to COVID-19	0	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

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TABLE 14.3__1.2.1.7

Overview of Treatment-Emergent Adverse Events and All Deaths After Discontinuation of Study Treatment by Time Period
Among Non-randomized Subjects
(SA1 Population)

Time Period	Placebo SC (N=27) n (%)	Risankizumab 180 mg SC (N=5) n (%)	Risankizumab 360 mg SC (N=0) n (%)	Risankizumab Total (N=5) n (%)	Risankizumab Rescue Therapy* (N=9) n (%)
91 days after last dose date to 140 days after last dose date					
Subjects with any treatment-emergent					
Adverse event (AE)	1 (3.7)	0	0	0	0
AE related to COVID-19	0	0	0	0	0
AE related to study drug according to the investigator	0	0	0	0	0
Severe AE	0	0	0	0	0
Serious AE	1 (3.7)	0	0	0	0
AE leading to discontinuation of study drug	0	0	0	0	0
AE leading to death	0	0	0	0	0
All deaths					
Deaths occurring <= 140 days after last dose of study drug	0	0	0	0	0
Deaths occurring > 140 days after last dose of study drug	0	0	0	0	0
Deaths related to COVID-19	0	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

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表4

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RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-000 SUB-STUDY 1
R&D/21/0085 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
Any adverse event	135 (73.4)	128 (71.5)	129 (72.1)	257 (71.8)	92 (61.3)
血液およびリンパ系障害	8 (4.3)	15 (8.4)	11 (6.1)	26 (7.3)	7 (4.7)
貧血	8 (4.3)	9 (5.0)	8 (4.5)	17 (4.7)	5 (3.3)
慢性疾患の貧血	0	1 (0.6)	0	1 (0.3)	0
鉄欠乏性貧血	0	2 (1.1)	2 (1.1)	4 (1.1)	2 (1.3)
白血球減少症	1 (0.5)	0	1 (0.6)	1 (0.3)	0
リンパ節症	0	1 (0.6)	0	1 (0.3)	0
リンパ球減少症	1 (0.5)	1 (0.6)	0	1 (0.3)	0
小球性貧血	0	1 (0.6)	0	1 (0.3)	0
骨髄抑制	0	0	1 (0.6)	1 (0.3)	0
好中球減少症	0	1 (0.6)	0	1 (0.3)	0
心臓障害	4 (2.2)	6 (3.4)	4 (2.2)	10 (2.8)	2 (1.3)
急性心筋梗塞	0	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
心臓障害 (Cont.)					
徐脈	1 (0.5)	1 (0.6)	0	1 (0.3)	0
左脚ブロック	0	0	1 (0.6)	1 (0.3)	0
心機能障害	0	0	1 (0.6)	1 (0.3)	0
心不全	1 (0.5)	0	0	0	0
急性心不全	0	1 (0.6)	0	1 (0.3)	0
うっ血性心不全	0	1 (0.6)	0	1 (0.3)	0
冠動脈疾患	0	0	0	0	1 (0.7)
冠動脈穿孔	0	0	0	0	1 (0.7)
期外収縮	1 (0.5)	1 (0.6)	0	1 (0.3)	0
虚血性心筋症	0	0	0	0	1 (0.7)
動悸	1 (0.5)	0	0	0	0
心膜嚢胞	0	1 (0.6)	0	1 (0.3)	0
心嚢液貯留	0	0	0	0	1 (0.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
心臓障害 (Cont.)					
洞性頻脈	0	1 (0.6)	0	1 (0.3)	0
上室性頻脈	0	1 (0.6)	0	1 (0.3)	0
頻脈	0	0	1 (0.6)	1 (0.3)	0
先天性、家族性および遺伝性障害	0	0	0	0	1 (0.7)
聴覚ニューロパチースペクトラム障害	0	0	0	0	1 (0.7)
耳および迷路障害	2 (1.1)	0	2 (1.1)	2 (0.6)	0
耳鳴	1 (0.5)	0	1 (0.6)	1 (0.3)	0
回転性めまい	1 (0.5)	0	0	0	0
頭位性回転性めまい	0	0	1 (0.6)	1 (0.3)	0
内分泌障害	2 (1.1)	1 (0.6)	1 (0.6)	2 (0.6)	0
副腎機能不全	1 (0.5)	0	0	0	0
自己免疫性甲状腺炎	0	1 (0.6)	0	1 (0.3)	0
甲状腺機能低下症	1 (0.5)	0	0	0	0

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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
内分泌障害 (Cont.)					
ステロイド離脱症候群	0	0	1 (0.6)	1 (0.3)	0
眼障害	4 (2.2)	5 (2.8)	4 (2.2)	9 (2.5)	5 (3.3)
眼瞼炎	1 (0.5)	0	0	0	0
白内障	0	1 (0.6)	0	1 (0.3)	0
結膜出血	0	0	1 (0.6)	1 (0.3)	0
アレルギー性結膜炎	0	1 (0.6)	0	1 (0.3)	0
複視	0	0	0	0	1 (0.7)
上強膜炎	0	0	1 (0.6)	1 (0.3)	0
眼脂	0	0	1 (0.6)	1 (0.3)	0
眼出血	0	0	0	0	1 (0.7)
眼痛	0	1 (0.6)	0	1 (0.3)	0
虹彩炎	0	0	1 (0.6)	1 (0.3)	1 (0.7)
黄斑変性	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
眼障害 (Cont.)					
眼充血	0	0	0	0	1 (0.7)
ぶどう膜炎	0	1 (0.6)	0	1 (0.3)	0
霧視	0	1 (0.6)	0	1 (0.3)	0
視力障害	1 (0.5)	0	0	0	1 (0.7)
硝子体浮遊物	1 (0.5)	0	0	0	0
胃腸障害	75 (40.8)	64 (35.8)	67 (37.4)	131 (36.6)	42 (28.0)
腹部膨満	2 (1.1)	1 (0.6)	3 (1.7)	4 (1.1)	0
腹部ヘルニア	2 (1.1)	0	0	0	0
腹部腫瘤	0	0	1 (0.6)	1 (0.3)	1 (0.7)
腹痛	13 (7.1)	8 (4.5)	9 (5.0)	17 (4.7)	5 (3.3)
下腹部痛	1 (0.5)	3 (1.7)	0	3 (0.8)	0
上腹部痛	1 (0.5)	1 (0.6)	3 (1.7)	4 (1.1)	3 (2.0)
腹部圧痛	0	0	2 (1.1)	2 (0.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
胃腸障害 (Cont.)					
後天性食道ウエッブ	0	0	1 (0.6)	1 (0.3)	0
裂肛	1 (0.5)	3 (1.7)	3 (1.7)	6 (1.7)	2 (1.3)
痔瘻	4 (2.2)	1 (0.6)	3 (1.7)	4 (1.1)	3 (2.0)
肛門失禁	0	0	0	0	1 (0.7)
肛門の炎症	0	0	1 (0.6)	1 (0.3)	0
肛門そう痒症	0	1 (0.6)	0	1 (0.3)	0
肛門狭窄	1 (0.5)	1 (0.6)	2 (1.1)	3 (0.8)	1 (0.7)
肛門潰瘍	0	0	1 (0.6)	1 (0.3)	0
口角口唇炎	0	1 (0.6)	0	1 (0.3)	0
肛門直腸不快感	1 (0.5)	0	0	0	0
肛門直腸障害	1 (0.5)	0	0	0	0
アフタ性潰瘍	3 (1.6)	2 (1.1)	4 (2.2)	6 (1.7)	0
胆汁酸吸収不良	0	2 (1.1)	0	2 (0.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
胃腸障害 (Cont.)					
結腸異形成	1 (0.5)	0	0	0	0
結腸瘻	1 (0.5)	0	0	0	0
便秘	7 (3.8)	7 (3.9)	1 (0.6)	8 (2.2)	3 (2.0)
クローン病	32 (17.4)	19 (10.6)	21 (11.7)	40 (11.2)	16 (10.7)
便意切迫	1 (0.5)	1 (0.6)	0	1 (0.3)	0
齲歯	2 (1.1)	2 (1.1)	2 (1.1)	4 (1.1)	0
下痢	10 (5.4)	6 (3.4)	4 (2.2)	10 (2.8)	3 (2.0)
口内乾燥	0	1 (0.6)	0	1 (0.3)	0
十二指腸炎	0	1 (0.6)	0	1 (0.3)	0
消化不良	3 (1.6)	4 (2.2)	2 (1.1)	6 (1.7)	0
小腸炎	0	1 (0.6)	0	1 (0.3)	0
腸管皮膚瘻	1 (0.5)	0	0	0	0
心窩部不快感	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
胃腸障害 (Cont.)					
鼓腸	0	2 (1.1)	0	2 (0.6)	0
食中毒	2 (1.1)	0	0	0	0
排便回数増加	3 (1.6)	4 (2.2)	1 (0.6)	5 (1.4)	0
胃炎	2 (1.1)	0	1 (0.6)	1 (0.3)	1 (0.7)
胃腸音異常	0	1 (0.6)	0	1 (0.3)	0
胃食道逆流性疾患	4 (2.2)	4 (2.2)	2 (1.1)	6 (1.7)	2 (1.3)
歯肉出血	0	2 (1.1)	0	2 (0.6)	0
歯肉痛	0	0	1 (0.6)	1 (0.3)	0
血便排泄	1 (0.5)	1 (0.6)	0	1 (0.3)	0
痔出血	0	1 (0.6)	0	1 (0.3)	0
痔核	0	2 (1.1)	2 (1.1)	4 (1.1)	2 (1.3)
血栓性痔核	1 (0.5)	0	0	0	0
裂孔ヘルニア	2 (1.1)	1 (0.6)	0	1 (0.3)	1 (0.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
胃腸障害 (Cont.)					
回腸狭窄	1 (0.5)	0	0	0	3 (2.0)
イレウス	0	1 (0.6)	2 (1.1)	3 (0.8)	1 (0.7)
腸閉塞	1 (0.5)	0	0	0	0
腸管穿孔	0	1 (0.6)	0	1 (0.3)	0
腸管狭窄	0	1 (0.6)	0	1 (0.3)	0
過敏性腸症候群	0	1 (0.6)	1 (0.6)	2 (0.6)	0
大腸狭窄	2 (1.1)	2 (1.1)	2 (1.1)	4 (1.1)	0
大腸ポリープ	0	0	2 (1.1)	2 (0.6)	1 (0.7)
口唇腫脹	1 (0.5)	0	0	0	0
口腔内潰瘍形成	0	1 (0.6)	0	1 (0.3)	0
悪心	13 (7.1)	9 (5.0)	4 (2.2)	13 (3.6)	4 (2.7)
食道食物嵌入	0	1 (0.6)	0	1 (0.3)	0
食道炎	0	0	0	0	1 (0.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
胃腸障害 (Cont.)					
口腔内不快感	0	1 (0.6)	0	1 (0.3)	0
口腔粘膜水疱形成	1 (0.5)	0	0	0	0
膵嚢胞	0	1 (0.6)	0	1 (0.3)	0
膵炎	0	0	1 (0.6)	1 (0.3)	0
腹膜障害	0	1 (0.6)	0	1 (0.3)	0
肛門周囲痛	1 (0.5)	1 (0.6)	0	1 (0.3)	1 (0.7)
蛋白漏出性胃腸症	0	0	1 (0.6)	1 (0.3)	0
偽性ポリポーシス	0	1 (0.6)	0	1 (0.3)	0
直腸出血	2 (1.1)	1 (0.6)	2 (1.1)	3 (0.8)	0
直腸狭窄	0	0	1 (0.6)	1 (0.3)	0
吐き戻し	0	0	0	0	1 (0.7)
唾液腺粘液嚢胞	1 (0.5)	0	0	0	0
小腸閉塞	0	1 (0.6)	3 (1.7)	4 (1.1)	1 (0.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
胃腸障害 (Cont.)					
亜イレウス	0	1 (0.6)	1 (0.6)	2 (0.6)	0
埋伏歯	0	0	0	0	1 (0.7)
歯痛	2 (1.1)	2 (1.1)	1 (0.6)	3 (0.8)	0
嘔吐	8 (4.3)	1 (0.6)	3 (1.7)	4 (1.1)	1 (0.7)
一般・全身障害および投与部位の状態	26 (14.1)	23 (12.8)	25 (14.0)	48 (13.4)	15 (10.0)
無力症	1 (0.5)	1 (0.6)	2 (1.1)	3 (0.8)	0
胸部不快感	1 (0.5)	0	0	0	0
胸痛	1 (0.5)	2 (1.1)	0	2 (0.6)	0
悪寒	1 (0.5)	0	0	0	1 (0.7)
疲労	4 (2.2)	7 (3.9)	5 (2.8)	12 (3.4)	0
高体温症	0	0	1 (0.6)	1 (0.3)	0
治癒不良	1 (0.5)	1 (0.6)	0	1 (0.3)	0
インフルエンザ様疾患	2 (1.1)	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
注射部位内出血	1 (0.5)	0	0	0	0
注射部位紅斑	5 (2.7)	7 (3.9)	7 (3.9)	14 (3.9)	6 (4.0)
注射部位過敏反応	0	0	1 (0.6)	1 (0.3)	0
注射部位硬結	1 (0.5)	0	0	0	0
注射部位結節	0	1 (0.6)	0	1 (0.3)	0
注射部位疼痛	2 (1.1)	0	1 (0.6)	1 (0.3)	2 (1.3)
注射部位そう痒感	0	0	0	0	1 (0.7)
注射部位発疹	0	0	1 (0.6)	1 (0.3)	1 (0.7)
注射部位反応	1 (0.5)	2 (1.1)	1 (0.6)	3 (0.8)	3 (2.0)
注射部位腫脹	1 (0.5)	0	2 (1.1)	2 (0.6)	0
注射部位蕁麻疹	0	1 (0.6)	1 (0.6)	2 (0.6)	0
注射部位小水疱	0	1 (0.6)	0	1 (0.3)	0
注射部位熱感	0	0	1 (0.6)	1 (0.3)	0

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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

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一般・全身障害および投与部位の状態 (Cont.)					
倦怠感	1 (0.5)	0	1 (0.6)	1 (0.3)	0
末梢性浮腫	1 (0.5)	0	0	0	2 (1.3)
疼痛	2 (1.1)	1 (0.6)	2 (1.1)	3 (0.8)	0
末梢腫脹	2 (1.1)	1 (0.6)	1 (0.6)	2 (0.6)	0
発熱	6 (3.3)	7 (3.9)	8 (4.5)	15 (4.2)	4 (2.7)
評価不能の事象	0	1 (0.6)	0	1 (0.3)	1 (0.7)
肝胆道系障害	2 (1.1)	4 (2.2)	6 (3.4)	10 (2.8)	1 (0.7)
硬化性胆管炎	0	0	1 (0.6)	1 (0.3)	0
胆石症	1 (0.5)	1 (0.6)	0	1 (0.3)	0
胆嚢ポリープ	0	0	1 (0.6)	1 (0.3)	0
肝機能異常	0	1 (0.6)	0	1 (0.3)	0
脂肪肝	0	2 (1.1)	2 (1.1)	4 (1.1)	1 (0.7)
肝腫大	0	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
肝胆道系障害 (Cont.)					
高ビリルビン血症	1 (0.5)	0	2 (1.1)	2 (0.6)	0
免疫系障害	3 (1.6)	2 (1.1)	4 (2.2)	6 (1.7)	3 (2.0)
アレルギー性浮腫	0	0	1 (0.6)	1 (0.3)	0
動物アレルギー	0	1 (0.6)	0	1 (0.3)	0
過敏症	1 (0.5)	0	1 (0.6)	1 (0.3)	1 (0.7)
季節性アレルギー	2 (1.1)	1 (0.6)	3 (1.7)	4 (1.1)	2 (1.3)
感染症および寄生虫症	74 (40.2)	60 (33.5)	61 (34.1)	121 (33.8)	42 (28.0)
腹部膿瘍	1 (0.5)	0	0	0	0
四肢膿瘍	1 (0.5)	2 (1.1)	1 (0.6)	3 (0.8)	1 (0.7)
アエロモナス感染	0	0	1 (0.6)	1 (0.3)	0
肛門膿瘍	3 (1.6)	0	3 (1.7)	3 (0.8)	2 (1.3)
肛門直腸蜂巣炎	1 (0.5)	0	0	0	0
虫垂炎	1 (0.5)	2 (1.1)	0	2 (0.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

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感染症および寄生虫症 (Cont.)					
細菌性関節炎	0	1 (0.6)	0	1 (0.3)	0
無症候性COVID－19	1 (0.5)	0	0	0	0
バクテリアルトランスロケーション	0	0	0	0	1 (0.7)
バルトリン腺炎	0	0	1 (0.6)	1 (0.3)	0
気管支炎	3 (1.6)	1 (0.6)	3 (1.7)	4 (1.1)	0
COVID－19	0	1 (0.6)	4 (2.2)	5 (1.4)	4 (2.7)
カンピロバクター感染	1 (0.5)	0	0	0	0
よう	1 (0.5)	1 (0.6)	0	1 (0.3)	0
クラミジア感染	1 (0.5)	0	0	0	0
クロストリジウム・ディフィシレ大腸炎	0	1 (0.6)	0	1 (0.3)	0
クロストリジウム・ディフィシレ感染	0	0	1 (0.6)	1 (0.3)	2 (1.3)
結膜炎	0	1 (0.6)	2 (1.1)	3 (0.8)	2 (1.3)
ウイルス性結膜炎	0	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
感染症および寄生虫症 (Cont.)					
クリプトスポリジウム感染	0	0	1 (0.6)	1 (0.3)	0
膀胱炎	1 (0.5)	0	2 (1.1)	2 (0.6)	0
憩室炎	3 (1.6)	0	0	0	0
耳感染	2 (1.1)	1 (0.6)	0	1 (0.3)	1 (0.7)
大腸菌感染	0	0	0	0	1 (0.7)
大腸菌性尿路感染	1 (0.5)	0	0	0	0
毛包炎	1 (0.5)	1 (0.6)	0	1 (0.3)	2 (1.3)
皮膚真菌感染	1 (0.5)	0	1 (0.6)	1 (0.3)	0
胃腸炎	4 (2.2)	3 (1.7)	4 (2.2)	7 (2.0)	1 (0.7)
大腸菌性胃腸炎	1 (0.5)	0	0	0	0
赤痢菌性胃腸炎	0	0	0	0	1 (0.7)
ウイルス性胃腸炎	6 (3.3)	5 (2.8)	2 (1.1)	7 (2.0)	1 (0.7)
消化管内細菌過剰増殖	0	1 (0.6)	0	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
感染症および寄生虫症 (Cont.)					
消化管感染	0	1 (0.6)	1 (0.6)	2 (0.6)	0
陰部ヘルペス	1 (0.5)	1 (0.6)	1 (0.6)	2 (0.6)	0
女性性器感染	0	0	1 (0.6)	1 (0.3)	0
歯肉炎	1 (0.5)	0	1 (0.6)	1 (0.3)	0
ヘリコバクター感染	0	1 (0.6)	0	1 (0.3)	0
単純ヘルペス	1 (0.5)	2 (1.1)	0	2 (0.6)	0
帯状疱疹	1 (0.5)	2 (1.1)	0	2 (0.6)	0
播種性ヒストプラスマ症	0	0	0	0	1 (0.7)
麦粒腫	0	0	1 (0.6)	1 (0.3)	0
感染性嚢腫	0	1 (0.6)	0	1 (0.3)	0
感染性胸水	0	0	1 (0.6)	1 (0.3)	0
インフルエンザ	6 (3.3)	4 (2.2)	1 (0.6)	5 (1.4)	3 (2.0)
腎感染	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
感染症および寄生虫症 (Cont.)					
喉頭炎	1 (0.5)	0	0	0	0
潜伏結核	1 (0.5)	0	2 (1.1)	2 (0.6)	0
肝膿瘍	0	0	1 (0.6)	1 (0.3)	0
下気道感染	2 (1.1)	0	0	0	1 (0.7)
伝染性軟属腫	1 (0.5)	0	0	0	0
ムンプス	0	1 (0.6)	0	1 (0.3)	0
爪感染	0	0	0	0	1 (0.7)
上咽頭炎	25 (13.6)	17 (9.5)	17 (9.5)	34 (9.5)	10 (6.7)
爪真菌症	0	0	1 (0.6)	1 (0.3)	0
口腔真菌感染	0	1 (0.6)	0	1 (0.3)	0
口腔ヘルペス	2 (1.1)	4 (2.2)	3 (1.7)	7 (2.0)	4 (2.7)
急性中耳炎	0	0	1 (0.6)	1 (0.3)	0
爪囲炎	2 (1.1)	2 (1.1)	0	2 (0.6)	1 (0.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
感染症および寄生虫症 (Cont.)					
腹膜炎	0	0	1 (0.6)	1 (0.3)	0
扁桃周囲膿瘍	0	0	1 (0.6)	1 (0.3)	0
咽頭炎	0	1 (0.6)	0	1 (0.3)	1 (0.7)
レンサ球菌性咽頭炎	1 (0.5)	1 (0.6)	3 (1.7)	4 (1.1)	0
肺炎	2 (1.1)	1 (0.6)	0	1 (0.3)	1 (0.7)
マイコプラズマ性肺炎	0	0	1 (0.6)	1 (0.3)	0
シュードモナス感染	1 (0.5)	0	0	0	0
腰筋膿瘍	1 (0.5)	0	0	0	0
歯髄炎	1 (0.5)	1 (0.6)	0	1 (0.3)	0
膿疱	0	2 (1.1)	0	2 (0.6)	0
腎盂炎	0	0	1 (0.6)	1 (0.3)	0
ウイルス性気道感染	0	0	2 (1.1)	2 (0.6)	0
鼻炎	1 (0.5)	0	0	0	1 (0.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
感染症および寄生虫症 (Cont.)					
ロタウイルス感染	1 (0.5)	0	0	0	0
サルモネラ症	0	1 (0.6)	0	1 (0.3)	0
敗血症	0	0	0	0	2 (1.3)
副鼻腔炎	3 (1.6)	0	2 (1.1)	2 (0.6)	1 (0.7)
皮膚感染	0	1 (0.6)	0	1 (0.3)	0
軟部組織感染	0	0	1 (0.6)	1 (0.3)	0
皮下組織膿瘍	1 (0.5)	0	0	0	0
股部白癬	0	0	1 (0.6)	1 (0.3)	0
白癬感染	1 (0.5)	1 (0.6)	1 (0.6)	2 (0.6)	0
扁桃炎	0	0	0	0	1 (0.7)
歯膿瘍	1 (0.5)	1 (0.6)	0	1 (0.3)	0
歯感染	0	1 (0.6)	0	1 (0.3)	0
気管炎	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
感染症および寄生虫症 (Cont.)					
卵管卵巣膿瘍	0	0	0	0	1 (0.7)
上気道感染	7 (3.8)	7 (3.9)	3 (1.7)	10 (2.8)	5 (3.3)
尿路感染	6 (3.3)	1 (0.6)	7 (3.9)	8 (2.2)	4 (2.7)
ウイルス感染	1 (0.5)	0	3 (1.7)	3 (0.8)	0
ウイルス性咽頭炎	0	0	1 (0.6)	1 (0.3)	1 (0.7)
ウイルス性発疹	0	1 (0.6)	0	1 (0.3)	0
ウイルス性上気道感染	1 (0.5)	2 (1.1)	0	2 (0.6)	1 (0.7)
外陰部腟カンジダ症	1 (0.5)	1 (0.6)	1 (0.6)	2 (0.6)	0
外陰腟真菌感染	0	0	1 (0.6)	1 (0.3)	0
ブドウ球菌性創感染	0	0	1 (0.6)	1 (0.3)	0
傷害、中毒および処置合併症	10 (5.4)	7 (3.9)	12 (6.7)	19 (5.3)	6 (4.0)
肛門損傷	0	0	1 (0.6)	1 (0.3)	0
吻合部狭窄	0	0	0	0	1 (0.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
傷害、中毒および処置合併症 (Cont.)					
動物咬傷	2 (1.1)	0	0	0	0
動物による引っかき傷	0	0	1 (0.6)	1 (0.3)	0
足関節部骨折	1 (0.5)	0	0	0	0
節足動物咬傷	1 (0.5)	0	1 (0.6)	1 (0.3)	0
骨挫傷	1 (0.5)	0	0	0	0
挫傷	0	2 (1.1)	0	2 (0.6)	0
上顆炎	1 (0.5)	0	0	0	0
転倒	1 (0.5)	1 (0.6)	2 (1.1)	3 (0.8)	0
足骨折	1 (0.5)	0	0	0	0
手骨折	0	1 (0.6)	1 (0.6)	2 (0.6)	0
熱射病	0	0	0	0	1 (0.7)
創部炎症	1 (0.5)	0	0	0	0
関節損傷	1 (0.5)	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
傷害、中毒および処置合併症 (Cont.)					
靭帯断裂	0	1 (0.6)	1 (0.6)	2 (0.6)	0
靭帯捻挫	0	0	0	0	1 (0.7)
四肢損傷	0	0	0	0	1 (0.7)
肉離れ	0	0	0	0	1 (0.7)
膝蓋骨骨折	0	0	1 (0.6)	1 (0.3)	0
皮膚裂傷	1 (0.5)	1 (0.6)	1 (0.6)	2 (0.6)	0
ストーマ部ヘルニア	0	1 (0.6)	0	1 (0.3)	0
腱断裂	0	0	0	0	1 (0.7)
熱傷	0	0	1 (0.6)	1 (0.3)	0
歯牙破折	1 (0.5)	2 (1.1)	0	2 (0.6)	1 (0.7)
上肢骨折	0	0	2 (1.1)	2 (0.6)	0
創傷	1 (0.5)	0	0	0	0
臨床検査	11 (6.0)	8 (4.5)	12 (6.7)	20 (5.6)	8 (5.3)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

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臨床検査 (Cont.)					
アラニンアミノトランスフェラーゼ増加	1 (0.5)	2 (1.1)	0	2 (0.6)	3 (2.0)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	0	1 (0.7)
血中アルカリホスファターゼ増加	0	0	1 (0.6)	1 (0.3)	0
血中ビリルビン増加	0	1 (0.6)	0	1 (0.3)	0
血中リン減少	0	1 (0.6)	0	1 (0.3)	2 (1.3)
血圧上昇	0	1 (0.6)	0	1 (0.3)	0
血中トリグリセリド増加	0	1 (0.6)	2 (1.1)	3 (0.8)	0
体温上昇	0	1 (0.6)	1 (0.6)	2 (0.6)	0
C一反応性蛋白増加	1 (0.5)	0	1 (0.6)	1 (0.3)	0
心電図QT延長	1 (0.5)	0	0	0	0
便中カルプロテクチン増加	1 (0.5)	0	0	0	0
γ一グルタミルトランスフェラーゼ増加	0	0	0	0	1 (0.7)
ヘモグロビン減少	0	1 (0.6)	0	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

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臨床検査 (Cont.)					
脂質増加	1 (0.5)	0	0	0	0
肝機能検査異常	1 (0.5)	0	0	0	0
肝機能検査値上昇	1 (0.5)	0	1 (0.6)	1 (0.3)	0
リンパ球数減少	1 (0.5)	0	0	0	0
結核菌群検査陽性	2 (1.1)	0	1 (0.6)	1 (0.3)	0
血小板数増加	0	1 (0.6)	0	1 (0.3)	0
尿潜血陽性	0	0	0	0	1 (0.7)
尿中ビリルビン増加	0	0	1 (0.6)	1 (0.3)	0
ビタミンD減少	1 (0.5)	0	1 (0.6)	1 (0.3)	0
体重減少	0	1 (0.6)	1 (0.6)	2 (0.6)	1 (0.7)
体重増加	1 (0.5)	1 (0.6)	3 (1.7)	4 (1.1)	2 (1.3)
白血球数減少	0	0	1 (0.6)	1 (0.3)	0
代謝および栄養障害	9 (4.9)	8 (4.5)	8 (4.5)	16 (4.5)	4 (2.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
代謝および栄養障害 (Cont.)					
異常体重減少	1 (0.5)	0	0	0	0
食欲減退	0	0	1 (0.6)	1 (0.3)	0
脱水	1 (0.5)	0	0	0	0
脂質異常症	2 (1.1)	0	0	0	0
葉酸欠乏	0	1 (0.6)	1 (0.6)	2 (0.6)	0
食物不耐性	1 (0.5)	0	1 (0.6)	1 (0.3)	0
耐糖能障害	0	0	1 (0.6)	1 (0.3)	0
痛風	0	0	0	0	1 (0.7)
高コレステロール血症	0	2 (1.1)	0	2 (0.6)	0
高血糖	0	1 (0.6)	0	1 (0.3)	0
高カリウム血症	0	1 (0.6)	0	1 (0.3)	0
高トリグリセリド血症	0	0	1 (0.6)	1 (0.3)	0
高尿酸血症	0	1 (0.6)	0	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
代謝および栄養障害 (Cont.)					
低アルブミン血症	0	0	1 (0.6)	1 (0.3)	0
低カルシウム血症	1 (0.5)	0	0	0	0
低血糖	0	0	1 (0.6)	1 (0.3)	0
低ナトリウム血症	1 (0.5)	0	0	0	1 (0.7)
鉄欠乏	1 (0.5)	1 (0.6)	0	1 (0.3)	0
代謝性アシドーシス	0	0	0	0	1 (0.7)
肥満	0	1 (0.6)	0	1 (0.3)	0
2型糖尿病	1 (0.5)	0	0	0	1 (0.7)
ビタミンD欠乏	1 (0.5)	2 (1.1)	1 (0.6)	3 (0.8)	0
筋骨格系および結合組織障害	37 (20.1)	31 (17.3)	38 (21.2)	69 (19.3)	16 (10.7)
関節痛	20 (10.9)	15 (8.4)	17 (9.5)	32 (8.9)	6 (4.0)
関節炎	3 (1.6)	2 (1.1)	3 (1.7)	5 (1.4)	0
関節障害	6 (3.3)	2 (1.1)	7 (3.9)	9 (2.5)	3 (2.0)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
筋骨格系および結合組織障害 (Cont.)					
背部痛	4 (2.2)	3 (1.7)	8 (4.5)	11 (3.1)	3 (2.0)
滑液包炎	0	2 (1.1)	2 (1.1)	4 (1.1)	0
結晶性関節障害	0	0	1 (0.6)	1 (0.3)	0
外骨腫	0	0	1 (0.6)	1 (0.3)	0
線維筋痛	0	1 (0.6)	0	1 (0.3)	0
瘻孔	0	1 (0.6)	0	1 (0.3)	0
瘻孔分泌物	1 (0.5)	0	1 (0.6)	1 (0.3)	0
肛径部痛	1 (0.5)	0	0	0	1 (0.7)
関節硬直	1 (0.5)	2 (1.1)	0	2 (0.6)	0
関節腫脹	0	0	1 (0.6)	1 (0.3)	0
筋痙縮	0	2 (1.1)	4 (2.2)	6 (1.7)	1 (0.7)
筋緊張	1 (0.5)	0	0	0	0
筋骨格系胸痛	1 (0.5)	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
筋骨格系および結合組織障害 (Cont.)					
筋骨格硬直	0	0	1 (0.6)	1 (0.3)	0
筋肉痛	4 (2.2)	3 (1.7)	0	3 (0.8)	0
頚部痛	1 (0.5)	0	1 (0.6)	1 (0.3)	1 (0.7)
変形性関節症	0	4 (2.2)	0	4 (1.1)	0
骨溶解	0	0	1 (0.6)	1 (0.3)	0
骨粗鬆症	1 (0.5)	0	0	0	0
四肢痛	1 (0.5)	1 (0.6)	4 (2.2)	5 (1.4)	1 (0.7)
多発性関節炎	1 (0.5)	0	0	0	0
関節リウマチ	0	0	0	0	1 (0.7)
肩回旋筋腱板症候群	1 (0.5)	0	0	0	0
仙腸骨炎	1 (0.5)	0	1 (0.6)	1 (0.3)	0
変形性脊椎症	0	1 (0.6)	0	1 (0.3)	0
脊椎関節障害	1 (0.5)	0	1 (0.6)	1 (0.3)	1 (0.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
筋骨格系および結合組織障害 (Cont.)					
滑液嚢腫	0	0	1 (0.6)	1 (0.3)	0
腱障害	0	1 (0.6)	1 (0.6)	2 (0.6)	0
腱炎	1 (0.5)	0	0	0	0
腱鞘炎	0	1 (0.6)	0	1 (0.3)	0
弾発指	1 (0.5)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	6 (3.3)	3 (1.7)	2 (1.1)	5 (1.4)	2 (1.3)
肛門性器疣贅	0	0	0	0	1 (0.7)
基底細胞癌	1 (0.5)	0	0	0	0
大腸腺腫	1 (0.5)	0	0	0	0
線維腫	1 (0.5)	0	0	0	0
限局性結節性過形成	0	1 (0.6)	0	1 (0.3)	0
HER2陽性乳癌	0	0	1 (0.6)	1 (0.3)	0
脂肪腫	1 (0.5)	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
肺腺癌	0	0	0	0	1 (0.7)
メラノサイト性母斑	0	1 (0.6)	0	1 (0.3)	0
骨転移	0	0	0	0	1 (0.7)
子宮平滑筋腫	2 (1.1)	1 (0.6)	0	1 (0.3)	0
神経系障害	23 (12.5)	19 (10.6)	15 (8.4)	34 (9.5)	9 (6.0)
味覚消失	0	1 (0.6)	0	1 (0.3)	0
無嗅覚	0	1 (0.6)	0	1 (0.3)	0
脳梗塞	1 (0.5)	0	0	0	0
浮動性めまい	3 (1.6)	2 (1.1)	1 (0.6)	3 (0.8)	3 (2.0)
頭部動揺	1 (0.5)	0	0	0	0
頭痛	11 (6.0)	9 (5.0)	11 (6.1)	20 (5.6)	4 (2.7)
感覚鈍麻	3 (1.6)	0	0	0	0
頭蓋内動脈瘤	0	0	0	0	1 (0.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
神経系障害 (Cont.)					
嗜眠	1 (0.5)	1 (0.6)	0	1 (0.3)	0
片頭痛	2 (1.1)	2 (1.1)	3 (1.7)	5 (1.4)	0
前兆を伴う片頭痛	0	0	1 (0.6)	1 (0.3)	1 (0.7)
多発性硬化症	1 (0.5)	0	0	0	0
眼振	0	0	0	0	1 (0.7)
錯感覚	1 (0.5)	0	2 (1.1)	2 (0.6)	0
部分発作	0	1 (0.6)	0	1 (0.3)	0
失神寸前の状態	0	1 (0.6)	0	1 (0.3)	0
神経根障害	1 (0.5)	0	0	0	1 (0.7)
反射異常	0	0	0	0	1 (0.7)
下肢静止不能症候群	0	2 (1.1)	0	2 (0.6)	0
網膜性片頭痛	0	0	0	0	1 (0.7)
坐骨神経痛	1 (0.5)	1 (0.6)	0	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
神経系障害 (Cont.)					
味覚障害	1 (0.5)	0	0	0	0
緊張性頭痛	1 (0.5)	0	0	0	0
精神障害	9 (4.9)	13 (7.3)	5 (2.8)	18 (5.0)	6 (4.0)
適応障害	0	0	1 (0.6)	1 (0.3)	0
不安	2 (1.1)	4 (2.2)	0	4 (1.1)	2 (1.3)
不安障害	0	0	1 (0.6)	1 (0.3)	0
注意欠如・多動性障害	0	0	1 (0.6)	1 (0.3)	0
抑うつ気分	0	1 (0.6)	0	1 (0.3)	0
うつ病	2 (1.1)	3 (1.7)	1 (0.6)	4 (1.1)	2 (1.3)
不眠症	4 (2.2)	5 (2.8)	0	5 (1.4)	1 (0.7)
易刺激性	0	1 (0.6)	0	1 (0.3)	0
パニック発作	1 (0.5)	0	0	0	1 (0.7)
睡眠障害	0	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
腎および尿路障害	2 (1.1)	7 (3.9)	2 (1.1)	9 (2.5)	1 (0.7)
急性腎障害	0	1 (0.6)	0	1 (0.3)	0
排尿困難	1 (0.5)	2 (1.1)	0	2 (0.6)	0
血尿	0	1 (0.6)	1 (0.6)	2 (0.6)	0
腎結石症	1 (0.5)	1 (0.6)	1 (0.6)	2 (0.6)	0
腎嚢胞	0	1 (0.6)	0	1 (0.3)	0
尿管結石症	0	1 (0.6)	0	1 (0.3)	0
尿閉	0	0	0	0	1 (0.7)
生殖系および乳房障害	6 (3.3)	4 (2.2)	4 (2.2)	8 (2.2)	1 (0.7)
バルトリン嚢腫	0	0	1 (0.6)	1 (0.3)	0
乳房線維化	1 (0.5)	0	0	0	0
子宮頚管ポリープ	1 (0.5)	0	0	0	0
子宮内膜症	0	1 (0.6)	0	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
生殖系および乳房障害 (Cont.)					
勃起不全	0	1 (0.6)	1 (0.6)	2 (0.6)	0
女性生殖器瘙	0	0	0	0	1 (0.7)
女性化乳房	0	1 (0.6)	0	1 (0.3)	0
月経過多	2 (1.1)	0	0	0	0
不規則月経	0	0	1 (0.6)	1 (0.3)	0
乳頭痛	0	1 (0.6)	0	1 (0.3)	0
希発月経	1 (0.5)	0	0	0	0
腟分泌物	1 (0.5)	0	0	0	0
腟出血	1 (0.5)	0	0	0	0
外陰腟乾燥	0	0	1 (0.6)	1 (0.3)	0
外陰腟紅斑	0	0	1 (0.6)	1 (0.3)	0
外陰腟そう痒症	1 (0.5)	0	0	0	0
呼吸器、胸郭および縦隔障害	12 (6.5)	11 (6.1)	11 (6.1)	22 (6.1)	7 (4.7)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
喘息	0	1 (0.6)	3 (1.7)	4 (1.1)	1 (0.7)
慢性閉塞性肺疾患	1 (0.5)	1 (0.6)	0	1 (0.3)	1 (0.7)
咳嗽	2 (1.1)	2 (1.1)	3 (1.7)	5 (1.4)	2 (1.3)
呼吸困難	1 (0.5)	1 (0.6)	1 (0.6)	2 (0.6)	0
鼻出血	1 (0.5)	2 (1.1)	2 (1.1)	4 (1.1)	0
鼻閉	1 (0.5)	0	0	0	0
鼻痂皮	1 (0.5)	0	0	0	0
口腔咽頭痛	3 (1.6)	1 (0.6)	1 (0.6)	2 (0.6)	2 (1.3)
胸膜痛	0	1 (0.6)	0	1 (0.3)	0
肺腫瘤	1 (0.5)	0	0	0	0
呼吸障害	1 (0.5)	0	0	0	0
アレルギー性鼻炎	0	1 (0.6)	1 (0.6)	2 (0.6)	1 (0.7)
鼻漏	0	0	3 (1.7)	3 (0.8)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
副鼻腔うっ血	0	1 (0.6)	0	1 (0.3)	0
睡眠時無呼吸症候群	0	0	0	0	1 (0.7)
咽喉刺激感	0	1 (0.6)	0	1 (0.3)	0
喘鳴	0	1 (0.6)	0	1 (0.3)	0
皮膚および皮下組織障害	30 (16.3)	34 (19.0)	15 (8.4)	49 (13.7)	18 (12.0)
ざ瘡	1 (0.5)	2 (1.1)	1 (0.6)	3 (0.8)	2 (1.3)
脱毛症	2 (1.1)	2 (1.1)	0	2 (0.6)	1 (0.7)
水疱	0	0	0	0	1 (0.7)
皮膚嚢腫	1 (0.5)	2 (1.1)	0	2 (0.6)	1 (0.7)
皮膚炎	0	1 (0.6)	1 (0.6)	2 (0.6)	0
アレルギー性皮膚炎	1 (0.5)	1 (0.6)	0	1 (0.3)	1 (0.7)
接触皮膚炎	2 (1.1)	1 (0.6)	0	1 (0.3)	1 (0.7)
皮膚筋炎	0	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
皮膚および皮下組織障害 (Cont.)					
薬疹	0	0	0	0	1 (0.7)
皮膚乾燥	3 (1.6)	2 (1.1)	3 (1.7)	5 (1.4)	0
湿疹	4 (2.2)	5 (2.8)	2 (1.1)	7 (2.0)	1 (0.7)
紅斑	2 (1.1)	1 (0.6)	0	1 (0.3)	0
結節性紅斑	1 (0.5)	1 (0.6)	0	1 (0.3)	1 (0.7)
毛質異常	1 (0.5)	0	0	0	0
汗腺炎	1 (0.5)	2 (1.1)	0	2 (0.6)	0
過角化	0	1 (0.6)	0	1 (0.3)	0
嵌入爪	1 (0.5)	2 (1.1)	0	2 (0.6)	0
神経皮膚炎	0	1 (0.6)	0	1 (0.3)	0
寝汗	1 (0.5)	0	0	0	0
口囲皮膚炎	0	1 (0.6)	0	1 (0.3)	0
光線過敏性反応	0	1 (0.6)	1 (0.6)	2 (0.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
皮膚および皮下組織障害 (Cont.)					
そう痒症	2 (1.1)	4 (2.2)	3 (1.7)	7 (2.0)	5 (3.3)
乾癬	1 (0.5)	0	0	0	1 (0.7)
壊疽性膿皮症	0	1 (0.6)	0	1 (0.3)	0
発疹	5 (2.7)	1 (0.6)	3 (1.7)	4 (1.1)	4 (2.7)
紅斑性皮疹	1 (0.5)	2 (1.1)	1 (0.6)	3 (0.8)	1 (0.7)
そう痒性皮疹	1 (0.5)	1 (0.6)	0	1 (0.3)	0
酒さ	0	1 (0.6)	1 (0.6)	2 (0.6)	0
脂漏性皮膚炎	1 (0.5)	0	0	0	0
皮膚剥脱	1 (0.5)	0	0	0	0
皮膚亀裂	0	0	0	0	1 (0.7)
皮膚病変	1 (0.5)	2 (1.1)	0	2 (0.6)	0
裂毛	1 (0.5)	0	0	0	0
蕁麻疹	2 (1.1)	3 (1.7)	1 (0.6)	4 (1.1)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
外科および内科処置	1 (0.5)	0	0	0	0
人工流産	1 (0.5)	0	0	0	0
血管障害	7 (3.8)	7 (3.9)	5 (2.8)	12 (3.4)	4 (2.7)
深部静脈血栓症	1 (0.5)	0	0	0	0
高血圧	4 (2.2)	5 (2.8)	4 (2.2)	9 (2.5)	3 (2.0)
低血圧	1 (0.5)	0	0	0	0
蒼白	0	0	0	0	1 (0.7)
レイノー現象	0	0	1 (0.6)	1 (0.3)	0
血栓性静脈炎	0	0	1 (0.6)	1 (0.3)	0
血栓症	1 (0.5)	0	0	0	0
静脈瘤	0	1 (0.6)	0	1 (0.3)	0
血管炎	0	1 (0.6)	0	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Subjects are counted once in each row, regardless of the number of events they may have had.
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Program Source Code: [redacted]

表5

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
Any adverse event	82 (77.4)	27 (87.1)	26 (78.8)	53 (82.8)	36 (59.0)
血液およびリンパ系障害	4 (3.8)	5 (16.1)	1 (3.0)	6 (9.4)	4 (6.6)
貧血	3 (2.8)	0	1 (3.0)	1 (1.6)	3 (4.9)
鉄欠乏性貧血	1 (0.9)	0	0	0	0
白血球減少症	0	1 (3.2)	0	1 (1.6)	0
リンパ節症	0	2 (6.5)	0	2 (3.1)	0
リンパ球増加症	0	0	0	0	1 (1.6)
リンパ球減少症	1 (0.9)	0	0	0	0
好中球減少症	0	0	0	0	1 (1.6)
正球性貧血	0	1 (3.2)	0	1 (1.6)	0
血小板減少症	0	1 (3.2)	0	1 (1.6)	0
心臓障害	1 (0.9)	3 (9.7)	0	3 (4.7)	0
急性心筋梗塞	0	1 (3.2)	0	1 (1.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
心臓障害 (Cont.)					
徐脈	0	1 (3.2)	0	1 (1.6)	0
右脚ブロック	0	1 (3.2)	0	1 (1.6)	0
冠動脈疾患	0	1 (3.2)	0	1 (1.6)	0
ストレス心筋症	0	1 (3.2)	0	1 (1.6)	0
頻脈	1 (0.9)	1 (3.2)	0	1 (1.6)	0
先天性、家族性および遺伝性障害	1 (0.9)	0	0	0	0
発育性股関節形成不全	1 (0.9)	0	0	0	0
耳および迷路障害	2 (1.9)	0	0	0	1 (1.6)
耳痛	1 (0.9)	0	0	0	0
回転性めまい	1 (0.9)	0	0	0	1 (1.6)
内分泌障害	1 (0.9)	0	0	0	0
甲状腺機能低下症	1 (0.9)	0	0	0	0
眼障害	2 (1.9)	1 (3.2)	2 (6.1)	3 (4.7)	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
眼障害 (Cont.)					
白内障	1 (0.9)	0	0	0	0
眼の炎症	0	1 (3.2)	0	1 (1.6)	0
虹彩炎	1 (0.9)	0	0	0	0
眼窩筋炎	0	0	1 (3.0)	1 (1.6)	0
網膜剥離	0	0	0	0	1 (1.6)
霧視	0	0	1 (3.0)	1 (1.6)	0
硝子体浮遊物	1 (0.9)	0	0	0	0
胃腸障害	50 (47.2)	16 (51.6)	12 (36.4)	28 (43.8)	15 (24.6)
腹部膨満	0	1 (3.2)	0	1 (1.6)	0
腹痛	6 (5.7)	5 (16.1)	2 (6.1)	7 (10.9)	1 (1.6)
下腹部痛	1 (0.9)	0	1 (3.0)	1 (1.6)	0
上腹部痛	2 (1.9)	0	0	0	0
腹部圧痛	0	0	1 (3.0)	1 (1.6)	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
胃腸障害 (Cont.)					
痔瘻	2 (1.9)	1 (3.2)	0	1 (1.6)	1 (1.6)
肛門直腸不快感	0	0	0	0	2 (3.3)
アフタ性潰瘍	2 (1.9)	1 (3.2)	0	1 (1.6)	0
胆汁酸吸収不良	1 (0.9)	0	0	0	0
便秘	1 (0.9)	1 (3.2)	1 (3.0)	2 (3.1)	0
クローン病	31 (29.2)	6 (19.4)	6 (18.2)	12 (18.8)	7 (11.5)
便意切迫	0	1 (3.2)	0	1 (1.6)	0
齲歯	0	0	0	0	1 (1.6)
下痢	2 (1.9)	1 (3.2)	1 (3.0)	2 (3.1)	0
憩室	0	0	1 (3.0)	1 (1.6)	0
消化不良	2 (1.9)	0	0	0	1 (1.6)
嚥下障害	0	0	0	0	2 (3.3)
腹膜垂炎	0	0	0	0	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
胃腸障害 (Cont.)					
鼓腸	0	0	1 (3.0)	1 (1.6)	0
食中毒	0	0	1 (3.0)	1 (1.6)	0
排便回数増加	1 (0.9)	1 (3.2)	1 (3.0)	2 (3.1)	0
胃炎	2 (1.9)	0	0	0	0
胃腸管瘻	1 (0.9)	0	0	0	0
胃腸の炎症	1 (0.9)	0	0	0	0
胃食道逆流性疾患	0	0	0	0	2 (3.3)
血便排泄	0	0	1 (3.0)	1 (1.6)	0
痔核	0	0	1 (3.0)	1 (1.6)	0
腸閉塞	1 (0.9)	0	0	0	0
腸管狭窄	0	0	0	0	1 (1.6)
大腸閉塞	0	1 (3.2)	0	1 (1.6)	0
大腸穿孔	0	1 (3.2)	0	1 (1.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
胃腸障害 (Cont.)					
口腔白斑症	0	0	1 (3.0)	1 (1.6)	0
悪心	4 (3.8)	4 (12.9)	1 (3.0)	5 (7.8)	1 (1.6)
直腸炎	1 (0.9)	0	1 (3.0)	1 (1.6)	0
直腸出血	0	1 (3.2)	1 (3.0)	2 (3.1)	1 (1.6)
埋伏歯	1 (0.9)	0	0	0	0
歯痛	2 (1.9)	0	0	0	0
嘔吐	1 (0.9)	2 (6.5)	0	2 (3.1)	0
一般・全身障害および投与部位の状態	12 (11.3)	11 (35.5)	3 (9.1)	14 (21.9)	7 (11.5)
無力症	1 (0.9)	0	0	0	0
胸部不快感	0	1 (3.2)	0	1 (1.6)	0
胸痛	0	2 (6.5)	0	2 (3.1)	1 (1.6)
悪寒	1 (0.9)	0	0	0	0
疲労	3 (2.8)	4 (12.9)	0	4 (6.3)	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
全身健康状態悪化	0	1 (3.2)	0	1 (1.6)	0
全身性浮腫	0	1 (3.2)	0	1 (1.6)	1 (1.6)
高体温症	1 (0.9)	0	0	0	0
インフルエンザ様疾患	0	1 (3.2)	0	1 (1.6)	0
注射部位内出血	0	1 (3.2)	0	1 (1.6)	0
注射部位紅斑	1 (0.9)	2 (6.5)	2 (6.1)	4 (6.3)	2 (3.3)
注射部位疼痛	1 (0.9)	1 (3.2)	0	1 (1.6)	0
注射部位蒼白	1 (0.9)	0	0	0	0
注射部位そう痒感	0	1 (3.2)	0	1 (1.6)	0
注射部位腫脹	1 (0.9)	0	0	0	1 (1.6)
末梢性浮腫	1 (0.9)	0	0	0	0
疼痛	1 (0.9)	0	0	0	0
末梢腫脹	0	0	1 (3.0)	1 (1.6)	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Subjects are counted once in each row, regardless of the number of events they may have had.
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Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
発熱	4 (3.8)	1 (3.2)	0	1 (1.6)	3 (4.9)
全身性炎症反応症候群	0	1 (3.2)	0	1 (1.6)	0
肝胆道系障害	1 (0.9)	0	1 (3.0)	1 (1.6)	0
胆石症	1 (0.9)	0	0	0	0
脂肪肝	0	0	1 (3.0)	1 (1.6)	0
免疫系障害	1 (0.9)	1 (3.2)	0	1 (1.6)	2 (3.3)
薬物過敏症	0	0	0	0	1 (1.6)
過敏症	1 (0.9)	0	0	0	1 (1.6)
季節性アレルギー	0	1 (3.2)	0	1 (1.6)	0
感染症および寄生虫症	36 (34.0)	12 (38.7)	17 (51.5)	29 (45.3)	16 (26.2)
腹部膿瘍	1 (0.9)	0	0	0	0
四肢膿瘍	1 (0.9)	0	0	0	0
肛門膿瘍	4 (3.8)	0	0	0	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
感染症および寄生虫症 (Cont.)					
無症候性COVID－19	1 (0.9)	0	0	0	0
気管支炎	0	2 (6.5)	0	2 (3.1)	2 (3.3)
ウイルス性気管支炎	0	0	1 (3.0)	1 (1.6)	0
COVID－19	3 (2.8)	0	0	0	2 (3.3)
COVID－19肺炎	1 (0.9)	0	0	0	0
蜂巣炎	1 (0.9)	0	0	0	0
クロストリジウム・ディフィシレ大腸炎	0	1 (3.2)	0	1 (1.6)	0
クロストリジウム・ディフィシレ感染	1 (0.9)	0	0	0	0
結膜炎	1 (0.9)	0	0	0	0
膀胱炎	0	0	1 (3.0)	1 (1.6)	1 (1.6)
耳感染	0	0	0	0	1 (1.6)
毛包炎	1 (0.9)	0	0	0	0
真菌感染	0	0	2 (6.1)	2 (3.1)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
感染症および寄生虫症 (Cont.)					
ウイルス性胃炎	0	0	0	0	1 (1.6)
胃腸炎	1 (0.9)	2 (6.5)	1 (3.0)	3 (4.7)	0
サルモネラ菌性胃腸炎	0	0	0	0	1 (1.6)
歯肉炎	1 (0.9)	0	0	0	0
帯状疱疹	0	1 (3.2)	0	1 (1.6)	1 (1.6)
インフルエンザ	2 (1.9)	2 (6.5)	1 (3.0)	3 (4.7)	0
迷路炎	1 (0.9)	0	0	0	0
潜伏結核	0	1 (3.2)	0	1 (1.6)	0
上咽頭炎	7 (6.6)	3 (9.7)	6 (18.2)	9 (14.1)	7 (11.5)
口腔真菌感染	1 (0.9)	0	0	0	0
口腔ヘルペス	1 (0.9)	0	0	0	1 (1.6)
精巣炎	1 (0.9)	0	0	0	0
咽頭炎	2 (1.9)	0	1 (3.0)	1 (1.6)	2 (3.3)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
感染症および寄生虫症 (Cont.)					
肺炎	1 (0.9)	0	0	0	0
膿尿	0	1 (3.2)	0	1 (1.6)	0
気道感染	1 (0.9)	0	0	0	0
細菌性気道感染	0	0	0	0	1 (1.6)
ウイルス性気道感染	0	0	1 (3.0)	1 (1.6)	0
敗血症	0	1 (3.2)	0	1 (1.6)	0
副鼻腔炎	2 (1.9)	1 (3.2)	0	1 (1.6)	1 (1.6)
扁桃炎	1 (0.9)	0	0	0	0
歯膿瘍	0	1 (3.2)	0	1 (1.6)	0
上気道感染	2 (1.9)	3 (9.7)	3 (9.1)	6 (9.4)	1 (1.6)
ウレアプラズマ感染	0	0	1 (3.0)	1 (1.6)	0
尿路感染	3 (2.8)	1 (3.2)	1 (3.0)	2 (3.1)	0
腟感染	0	0	1 (3.0)	1 (1.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
感染症および寄生虫症 (Cont.)					
ウイルス感染	1 (0.9)	1 (3.2)	0	1 (1.6)	0
ウイルス性発疹	1 (0.9)	0	0	0	0
ウイルス性上気道感染	3 (2.8)	0	0	0	1 (1.6)
エルシニア感染	0	1 (3.2)	0	1 (1.6)	0
傷害、中毒および処置合併症	3 (2.8)	3 (9.7)	2 (6.1)	5 (7.8)	3 (4.9)
足関節部骨折	0	0	0	0	1 (1.6)
節足動物咬傷	1 (0.9)	0	0	0	0
挫傷	0	0	1 (3.0)	1 (1.6)	0
前腕骨折	1 (0.9)	0	0	0	0
胃腸吻合部狭窄	0	1 (3.2)	0	1 (1.6)	0
手骨折	0	0	0	0	1 (1.6)
関節脱臼	0	0	0	0	1 (1.6)
半月板損傷	0	1 (3.2)	0	1 (1.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
傷害、中毒および処置合併症 (Cont.)					
処置による腸管穿孔	0	0	1 (3.0)	1 (1.6)	0
肋骨骨折	0	1 (3.2)	0	1 (1.6)	0
瘢痕	1 (0.9)	0	0	0	0
臨床検査	5 (4.7)	2 (6.5)	0	2 (3.1)	3 (4.9)
血中鉄減少	1 (0.9)	0	0	0	0
血中リン減少	0	0	0	0	1 (1.6)
心電図QT延長	1 (0.9)	0	0	0	0
心電図異常T波	0	0	0	0	1 (1.6)
ヘモグロビン減少	1 (0.9)	0	0	0	0
肝酵素上昇	1 (0.9)	0	0	0	0
ビタミンB12減少	1 (0.9)	1 (3.2)	0	1 (1.6)	0
体重減少	1 (0.9)	1 (3.2)	0	1 (1.6)	0
体重増加	0	0	0	0	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
代謝および栄養障害	3 (2.8)	5 (16.1)	0	5 (7.8)	3 (4.9)
食欲減退	1 (0.9)	0	0	0	0
糖尿病	0	0	0	0	1 (1.6)
脂質異常症	0	1 (3.2)	0	1 (1.6)	0
耐糖能障害	0	1 (3.2)	0	1 (1.6)	0
低カルシウム血症	1 (0.9)	0	0	0	0
低フェリチン血症	0	0	0	0	1 (1.6)
低カリウム血症	1 (0.9)	3 (9.7)	0	3 (4.7)	0
低マグネシウム血症	1 (0.9)	1 (3.2)	0	1 (1.6)	0
鉄欠乏	0	0	0	0	1 (1.6)
2型糖尿病	0	1 (3.2)	0	1 (1.6)	0
筋骨格系および結合組織障害	13 (12.3)	7 (22.6)	6 (18.2)	13 (20.3)	11 (18.0)
関節痛	1 (0.9)	3 (9.7)	4 (12.1)	7 (10.9)	4 (6.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
筋骨格系および結合組織障害 (Cont.)					
関節障害	0	1 (3.2)	1 (3.0)	2 (3.1)	1 (1.6)
背部痛	4 (3.8)	1 (3.2)	2 (6.1)	3 (4.7)	2 (3.3)
滑液包炎	0	1 (3.2)	0	1 (1.6)	0
腱付着部症	1 (0.9)	0	0	0	0
大腿骨寛骨臼インピンジメント	1 (0.9)	0	0	0	0
瘻孔分泌物	1 (0.9)	0	0	0	1 (1.6)
関節腫脹	1 (0.9)	1 (3.2)	0	1 (1.6)	0
筋緊張	0	1 (3.2)	0	1 (1.6)	0
筋攣縮	0	1 (3.2)	0	1 (1.6)	0
筋骨格硬直	0	0	0	0	2 (3.3)
筋肉痛	0	0	0	0	1 (1.6)
頚部痛	1 (0.9)	0	0	0	0
四肢痛	2 (1.9)	0	1 (3.0)	1 (1.6)	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
筋骨格系および結合組織障害 (Cont.)					
顎痛	0	1 (3.2)	0	1 (1.6)	0
脊椎痛	0	1 (3.2)	0	1 (1.6)	0
腱炎	0	1 (3.2)	0	1 (1.6)	0
弾発指	1 (0.9)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0	1 (1.6)
子宮平滑筋腫	0	0	0	0	1 (1.6)
神経系障害	7 (6.6)	4 (12.9)	4 (12.1)	8 (12.5)	2 (3.3)
失語症	1 (0.9)	0	0	0	0
浮動性めまい	1 (0.9)	1 (3.2)	0	1 (1.6)	0
脳症	0	1 (3.2)	0	1 (1.6)	0
頭痛	4 (3.8)	1 (3.2)	4 (12.1)	5 (7.8)	1 (1.6)
感覚鈍麻	0	1 (3.2)	0	1 (1.6)	1 (1.6)
嗜眠	0	1 (3.2)	0	1 (1.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
神経系障害 (Cont.)					
片頭痛	0	0	0	0	1 (1.6)
痙攣発作	1 (0.9)	1 (3.2)	0	1 (1.6)	0
精神障害	7 (6.6)	7 (22.6)	0	7 (10.9)	2 (3.3)
アルコール離脱症候群	1 (0.9)	0	0	0	0
不安	2 (1.9)	0	0	0	0
注意欠如・多動性障害	0	0	0	0	1 (1.6)
錯乱状態	0	1 (3.2)	0	1 (1.6)	0
抑うつ気分	0	0	0	0	1 (1.6)
うつ病	3 (2.8)	1 (3.2)	0	1 (1.6)	1 (1.6)
不眠症	0	3 (9.7)	0	3 (4.7)	0
易刺激性	1 (0.9)	1 (3.2)	0	1 (1.6)	0
ストレス	0	1 (3.2)	0	1 (1.6)	0
腎および尿路障害	3 (2.8)	0	1 (3.0)	1 (1.6)	2 (3.3)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
腎および尿路障害 (Cont.)					
高窒素血症	0	0	0	0	1 (1.6)
尿路結石	0	0	0	0	1 (1.6)
排尿困難	1 (0.9)	0	0	0	1 (1.6)
血尿	0	0	1 (3.0)	1 (1.6)	0
蛋白尿	0	0	0	0	1 (1.6)
腎嚢胞	1 (0.9)	0	0	0	0
腎機能障害	1 (0.9)	0	0	0	0
腎臓痛	0	0	0	0	1 (1.6)
排尿躊躇	0	0	0	0	1 (1.6)
生殖系および乳房障害	2 (1.9)	0	2 (6.1)	2 (3.1)	3 (4.9)
無月経	1 (0.9)	0	0	0	0
萎縮性外陰腟炎	0	0	1 (3.0)	1 (1.6)	0
乳房圧痛	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
生殖系および乳房障害 (Cont.)					
月経困難症	0	0	0	0	2 (3.3)
女性生殖器瘙	0	0	1 (3.0)	1 (1.6)	0
月経過多	0	0	0	0	1 (1.6)
不規則月経	0	0	0	0	1 (1.6)
多嚢胞性卵巣	0	0	0	0	1 (1.6)
腟出血	1 (0.9)	0	0	0	0
呼吸器、胸郭および縦隔障害	2 (1.9)	4 (12.9)	2 (6.1)	6 (9.4)	5 (8.2)
急性呼吸不全	0	1 (3.2)	0	1 (1.6)	0
喘息クリーゼ	0	0	0	0	1 (1.6)
咳嗽	0	0	1 (3.0)	1 (1.6)	1 (1.6)
呼吸困難	0	2 (6.5)	0	2 (3.1)	0
過換気	0	1 (3.2)	0	1 (1.6)	0
口腔咽頭痛	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
副鼻腔分泌過多	1 (0.9)	0	0	0	0
胸膜痛	0	0	0	0	1 (1.6)
湿性咳嗽	0	0	0	0	1 (1.6)
肺塞栓症	0	0	0	0	1 (1.6)
呼吸障害	0	0	1 (3.0)	1 (1.6)	0
皮膚および皮下組織障害	13 (12.3)	4 (12.9)	4 (12.1)	8 (12.5)	6 (9.8)
脱毛症	1 (0.9)	0	1 (3.0)	1 (1.6)	1 (1.6)
皮膚嚢腫	2 (1.9)	0	0	0	0
アレルギー性皮膚炎	0	0	0	0	1 (1.6)
接触皮膚炎	0	0	0	0	1 (1.6)
乾癬様皮膚炎	0	0	1 (3.0)	1 (1.6)	0
皮膚乾燥	1 (0.9)	0	0	0	0
湿疹	0	0	1 (3.0)	1 (1.6)	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
皮膚および皮下組織障害 (Cont.)					
紅斑	0	1 (3.2)	1 (3.0)	2 (3.1)	0
汗腺炎	2 (1.9)	0	0	0	0
間擦疹	1 (0.9)	0	0	0	0
寝汗	2 (1.9)	0	0	0	0
そう痒症	0	0	0	0	1 (1.6)
乾癬	0	1 (3.2)	1 (3.0)	2 (3.1)	0
発疹	1 (0.9)	2 (6.5)	1 (3.0)	3 (4.7)	1 (1.6)
脂漏性皮膚炎	1 (0.9)	0	0	0	0
皮膚変色	1 (0.9)	0	0	0	0
皮膚病変	1 (0.9)	0	0	0	0
皮膚腫瘤	1 (0.9)	0	0	0	0
中毒性皮疹	1 (0.9)	0	0	0	0
蕁麻疹	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
血管障害	5 (4.7)	1 (3.2)	0	1 (1.6)	1 (1.6)
深部静脈血栓症	1 (0.9)	0	0	0	0
潮紅	2 (1.9)	0	0	0	0
血腫	1 (0.9)	0	0	0	0
高血圧	0	1 (3.2)	0	1 (1.6)	1 (1.6)
低血圧	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

表6

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
Any adverse event	46 (25.0)	49 (27.4)	45 (25.1)	94 (26.3)	26 (17.3)
血液およびリンパ系障害	2 (1.1)	3 (1.7)	2 (1.1)	5 (1.4)	0
貧血	2 (1.1)	1 (0.6)	1 (0.6)	2 (0.6)	0
白血球減少症	0	0	1 (0.6)	1 (0.3)	0
リンパ節症	0	1 (0.6)	0	1 (0.3)	0
リンパ球減少症	1 (0.5)	0	0	0	0
好中球減少症	0	1 (0.6)	0	1 (0.3)	0
心臓障害	1 (0.5)	1 (0.6)	0	1 (0.3)	0
動悸	1 (0.5)	0	0	0	0
洞性頻脈	0	1 (0.6)	0	1 (0.3)	0
眼障害	2 (1.1)	0	0	0	0
視力障害	1 (0.5)	0	0	0	0
硝子体浮遊物	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
胃腸障害	15 (8.2)	14 (7.8)	4 (2.2)	18 (5.0)	4 (2.7)
腹部膨満	1 (0.5)	0	1 (0.6)	1 (0.3)	0
腹痛	1 (0.5)	3 (1.7)	1 (0.6)	4 (1.1)	0
下腹部痛	0	2 (1.1)	0	2 (0.6)	0
痔瘻	1 (0.5)	0	0	0	0
肛門狭窄	0	0	0	0	1 (0.7)
便秘	1 (0.5)	2 (1.1)	0	2 (0.6)	0
クローン病	6 (3.3)	4 (2.2)	1 (0.6)	5 (1.4)	1 (0.7)
下痢	3 (1.6)	1 (0.6)	0	1 (0.3)	1 (0.7)
消化不良	0	1 (0.6)	0	1 (0.3)	0
鼓腸	0	1 (0.6)	0	1 (0.3)	0
イレウス	0	1 (0.6)	0	1 (0.3)	0
腸閉塞	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
胃腸障害 (Cont.)					
口唇腫脹	1 (0.5)	0	0	0	0
口腔内潰瘍形成	0	1 (0.6)	0	1 (0.3)	0
悪心	1 (0.5)	3 (1.7)	1 (0.6)	4 (1.1)	1 (0.7)
直腸出血	1 (0.5)	0	0	0	0
直腸狭窄	0	0	1 (0.6)	1 (0.3)	0
嘔吐	1 (0.5)	0	1 (0.6)	1 (0.3)	0
一般・全身障害および投与部位の状態	8 (4.3)	12 (6.7)	11 (6.1)	23 (6.4)	8 (5.3)
疲労	0	4 (2.2)	1 (0.6)	5 (1.4)	0
治癒不良	1 (0.5)	0	0	0	0
注射部位内出血	1 (0.5)	0	0	0	0
注射部位紅斑	4 (2.2)	7 (3.9)	6 (3.4)	13 (3.6)	6 (4.0)
注射部位過敏反応	0	0	1 (0.6)	1 (0.3)	0
注射部位硬結	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
注射部位結節	0	1 (0.6)	0	1 (0.3)	0
注射部位疼痛	1 (0.5)	0	0	0	2 (1.3)
注射部位そう痒感	0	0	0	0	1 (0.7)
注射部位発疹	0	0	1 (0.6)	1 (0.3)	1 (0.7)
注射部位反応	1 (0.5)	2 (1.1)	0	2 (0.6)	2 (1.3)
注射部位腫脹	1 (0.5)	0	2 (1.1)	2 (0.6)	0
注射部位蕁麻疹	0	1 (0.6)	1 (0.6)	2 (0.6)	0
注射部位小水疱	0	1 (0.6)	0	1 (0.3)	0
注射部位熱感	0	0	1 (0.6)	1 (0.3)	0
疼痛	0	1 (0.6)	0	1 (0.3)	0
発熱	0	1 (0.6)	2 (1.1)	3 (0.8)	0
肝胆道系障害	1 (0.5)	0	2 (1.1)	2 (0.6)	0
高ビリルビン血症	1 (0.5)	0	2 (1.1)	2 (0.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
免疫系障害	0	0	2 (1.1)	2 (0.6)	1 (0.7)
過敏症	0	0	1 (0.6)	1 (0.3)	1 (0.7)
季節性アレルギー	0	0	1 (0.6)	1 (0.3)	0
感染症および寄生虫症	15 (8.2)	10 (5.6)	17 (9.5)	27 (7.5)	9 (6.0)
四肢膿瘍	0	0	1 (0.6)	1 (0.3)	0
肛門膿瘍	1 (0.5)	0	0	0	0
細菌性関節炎	0	1 (0.6)	0	1 (0.3)	0
バルトリン腺炎	0	0	1 (0.6)	1 (0.3)	0
気管支炎	0	0	1 (0.6)	1 (0.3)	0
クロストリジウム・ディフィシレ大腸炎	0	1 (0.6)	0	1 (0.3)	0
クロストリジウム・ディフィシレ感染	0	0	1 (0.6)	1 (0.3)	2 (1.3)
膀胱炎	1 (0.5)	0	0	0	0
皮膚真菌感染	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
感染症および寄生虫症 (Cont.)					
胃腸炎	0	0	1 (0.6)	1 (0.3)	0
赤痢菌性胃腸炎	0	0	0	0	1 (0.7)
ウイルス性胃腸炎	2 (1.1)	0	0	0	0
陰部ヘルペス	0	1 (0.6)	0	1 (0.3)	0
帯状疱疹	0	2 (1.1)	0	2 (0.6)	0
播種性ヒストプラスマ症	0	0	0	0	1 (0.7)
感染性胸水	0	0	1 (0.6)	1 (0.3)	0
インフルエンザ	0	1 (0.6)	0	1 (0.3)	1 (0.7)
喉頭炎	1 (0.5)	0	0	0	0
潜伏結核	0	0	1 (0.6)	1 (0.3)	0
肝膿瘍	0	0	1 (0.6)	1 (0.3)	0
下気道感染	1 (0.5)	0	0	0	0
上咽頭炎	2 (1.1)	3 (1.7)	5 (2.8)	8 (2.2)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term
Among Randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
感染症および寄生虫症 (Cont.)					
口腔ヘルペス	0	1 (0.6)	0	1 (0.3)	1 (0.7)
爪囲炎	1 (0.5)	2 (1.1)	0	2 (0.6)	0
咽頭炎	0	1 (0.6)	0	1 (0.3)	0
肺炎	1 (0.5)	0	0	0	0
ウイルス性気道感染	0	0	1 (0.6)	1 (0.3)	0
敗血症	0	0	0	0	1 (0.7)
副鼻腔炎	1 (0.5)	0	2 (1.1)	2 (0.6)	0
皮下組織膿瘍	1 (0.5)	0	0	0	0
股部白癬	0	0	1 (0.6)	1 (0.3)	0
白癬感染	0	0	1 (0.6)	1 (0.3)	0
扁桃炎	0	0	0	0	1 (0.7)
歯膿瘍	1 (0.5)	1 (0.6)	0	1 (0.3)	0
気管炎	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
感染症および寄生虫症 (Cont.)					
上気道感染	2 (1.1)	1 (0.6)	0	1 (0.3)	0
尿路感染	1 (0.5)	0	0	0	1 (0.7)
ウイルス感染	0	0	1 (0.6)	1 (0.3)	0
ウイルス性咽頭炎	0	0	1 (0.6)	1 (0.3)	0
外陰部腟カンジダ症	1 (0.5)	0	0	0	0
臨床検査	6 (3.3)	3 (1.7)	5 (2.8)	8 (2.2)	0
アラニンアミノトランスフェラーゼ増加	1 (0.5)	1 (0.6)	0	1 (0.3)	0
血中トリグリセリド増加	0	0	1 (0.6)	1 (0.3)	0
体温上昇	0	1 (0.6)	0	1 (0.3)	0
C－反応性蛋白増加	1 (0.5)	0	0	0	0
便中カルプロテクチン増加	1 (0.5)	0	0	0	0
肝機能検査異常	1 (0.5)	0	0	0	0
肝機能検査値上昇	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
臨床検査 (Cont.)					
リンパ球数減少	1 (0.5)	0	0	0	0
体重増加	1 (0.5)	1 (0.6)	3 (1.7)	4 (1.1)	0
白血球数減少	0	0	1 (0.6)	1 (0.3)	0
代謝および栄養障害	0	1 (0.6)	1 (0.6)	2 (0.6)	1 (0.7)
高コレステロール血症	0	1 (0.6)	0	1 (0.3)	0
高トリグリセリド血症	0	0	1 (0.6)	1 (0.3)	0
2型糖尿病	0	0	0	0	1 (0.7)
筋骨格系および結合組織障害	6 (3.3)	6 (3.4)	7 (3.9)	13 (3.6)	0
関節痛	4 (2.2)	2 (1.1)	4 (2.2)	6 (1.7)	0
関節炎	0	1 (0.6)	0	1 (0.3)	0
関節障害	1 (0.5)	1 (0.6)	1 (0.6)	2 (0.6)	0
背部痛	0	0	1 (0.6)	1 (0.3)	0
線維筋痛	0	1 (0.6)	0	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
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Subjects are counted once in each row, regardless of the number of events they may have had.
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Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
筋骨格系および結合組織障害 (Cont.)					
筋痙縮	0	1 (0.6)	2 (1.1)	3 (0.8)	0
筋肉痛	0	1 (0.6)	0	1 (0.3)	0
変形性関節症	0	1 (0.6)	0	1 (0.3)	0
多発性関節炎	1 (0.5)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.5)	0	0	0	0
大腸腺腫	1 (0.5)	0	0	0	0
神経系障害	2 (1.1)	6 (3.4)	2 (1.1)	8 (2.2)	4 (2.7)
浮動性めまい	1 (0.5)	1 (0.6)	0	1 (0.3)	1 (0.7)
頭痛	0	5 (2.8)	1 (0.6)	6 (1.7)	2 (1.3)
片頭痛	1 (0.5)	0	1 (0.6)	1 (0.3)	0
前兆を伴う片頭痛	0	0	0	0	1 (0.7)
多発性硬化症	1 (0.5)	0	0	0	0
精神障害	0	1 (0.6)	1 (0.6)	2 (0.6)	2 (1.3)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
精神障害 (Cont.)					
不安	0	1 (0.6)	0	1 (0.3)	0
不安障害	0	0	1 (0.6)	1 (0.3)	0
不眠症	0	0	0	0	1 (0.7)
パニック発作	0	0	0	0	1 (0.7)
腎および尿路障害	1 (0.5)	3 (1.7)	0	3 (0.8)	0
排尿困難	1 (0.5)	2 (1.1)	0	2 (0.6)	0
血尿	0	1 (0.6)	0	1 (0.3)	0
生殖系および乳房障害	1 (0.5)	0	1 (0.6)	1 (0.3)	0
勃起不全	0	0	1 (0.6)	1 (0.3)	0
腟分泌物	1 (0.5)	0	0	0	0
呼吸器、胸郭および縦隔障害	3 (1.6)	0	1 (0.6)	1 (0.3)	1 (0.7)
咳嗽	1 (0.5)	0	0	0	0
鼻痂皮	1 (0.5)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
口腔咽頭痛	1 (0.5)	0	1 (0.6)	1 (0.3)	1 (0.7)
皮膚および皮下組織障害	7 (3.8)	10 (5.6)	9 (5.0)	19 (5.3)	7 (4.7)
ざ瘡	0	0	1 (0.6)	1 (0.3)	1 (0.7)
脱毛症	0	0	0	0	1 (0.7)
アレルギー性皮膚炎	1 (0.5)	0	0	0	1 (0.7)
皮膚筋炎	0	0	1 (0.6)	1 (0.3)	0
皮膚乾燥	1 (0.5)	1 (0.6)	1 (0.6)	2 (0.6)	0
湿疹	2 (1.1)	2 (1.1)	1 (0.6)	3 (0.8)	0
紅斑	1 (0.5)	1 (0.6)	0	1 (0.3)	0
神経皮膚炎	0	1 (0.6)	0	1 (0.3)	0
口囲皮膚炎	0	1 (0.6)	0	1 (0.3)	0
光線過敏性反応	0	1 (0.6)	1 (0.6)	2 (0.6)	0
そう痒症	1 (0.5)	2 (1.1)	2 (1.1)	4 (1.1)	3 (2.0)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.1.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=184) n (%)	Risankizumab 180 mg SC (N=179) n (%)	Risankizumab 360 mg SC (N=179) n (%)	Risankizumab Total (N=358) n (%)	Risankizumab Rescue Therapy* (N=150) n (%)
皮膚および皮下組織障害 (Cont.)					
乾癬	0	0	0	0	1 (0.7)
発疹	2 (1.1)	0	1 (0.6)	1 (0.3)	1 (0.7)
紅斑性皮疹	0	0	1 (0.6)	1 (0.3)	0
そう痒性皮疹	0	1 (0.6)	0	1 (0.3)	0
皮膚亀裂	0	0	0	0	1 (0.7)
皮膚病変	0	1 (0.6)	0	1 (0.3)	0
蕁麻疹	0	2 (1.1)	1 (0.6)	3 (0.8)	0
血管障害	1 (0.5)	0	1 (0.6)	1 (0.3)	0
高血圧	1 (0.5)	0	1 (0.6)	1 (0.3)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

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表7

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STUDY M16-000 SUB-STUDY 1
R&D/21/0085 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 6

TABLE 14.3__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
Any adverse event	20 (18.9)	9 (29.0)	10 (30.3)	19 (29.7)	13 (21.3)
血液およびリンパ系障害	0	0	0	0	1 (1.6)
リンパ球増加症	0	0	0	0	1 (1.6)
好中球減少症	0	0	0	0	1 (1.6)
耳および迷路障害	0	0	0	0	1 (1.6)
回転性めまい	0	0	0	0	1 (1.6)
眼障害	0	0	1 (3.0)	1 (1.6)	0
霧視	0	0	1 (3.0)	1 (1.6)	0
胃腸障害	12 (11.3)	1 (3.2)	3 (9.1)	4 (6.3)	0
腹痛	2 (1.9)	0	1 (3.0)	1 (1.6)	0
下腹部痛	0	0	1 (3.0)	1 (1.6)	0
クローン病	9 (8.5)	0	1 (3.0)	1 (1.6)	0
下痢	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
胃腸障害 (Cont.)					
排便回数増加	0	0	1 (3.0)	1 (1.6)	0
悪心	0	1 (3.2)	0	1 (1.6)	0
直腸出血	0	0	1 (3.0)	1 (1.6)	0
一般・全身障害および投与部位の状態	3 (2.8)	4 (12.9)	1 (3.0)	5 (7.8)	2 (3.3)
疲労	0	1 (3.2)	0	1 (1.6)	0
注射部位紅斑	1 (0.9)	2 (6.5)	1 (3.0)	3 (4.7)	2 (3.3)
注射部位疼痛	1 (0.9)	1 (3.2)	0	1 (1.6)	0
注射部位蒼白	1 (0.9)	0	0	0	0
注射部位そう痒感	0	1 (3.2)	0	1 (1.6)	0
注射部位腫脹	1 (0.9)	0	0	0	1 (1.6)
発熱	1 (0.9)	0	0	0	0
肝胆道系障害	1 (0.9)	0	0	0	0
胆石症	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
免疫系障害	0	0	0	0	1 (1.6)
過敏症	0	0	0	0	1 (1.6)
感染症および寄生虫症	5 (4.7)	2 (6.5)	3 (9.1)	5 (7.8)	2 (3.3)
肛門膿瘍	1 (0.9)	0	0	0	0
気管支炎	0	1 (3.2)	0	1 (1.6)	1 (1.6)
ウイルス性気管支炎	0	0	1 (3.0)	1 (1.6)	0
耳感染	0	0	0	0	1 (1.6)
真菌感染	0	0	1 (3.0)	1 (1.6)	0
ウイルス性胃炎	0	0	0	0	1 (1.6)
帯状疱疹	0	1 (3.2)	0	1 (1.6)	0
上咽頭炎	2 (1.9)	0	1 (3.0)	1 (1.6)	1 (1.6)
精巣炎	1 (0.9)	0	0	0	0
副鼻腔炎	0	0	0	0	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
感染症および寄生虫症 (Cont.)					
扁桃炎	1 (0.9)	0	0	0	0
尿路感染	1 (0.9)	0	0	0	0
ウイルス性上気道感染	2 (1.9)	0	0	0	0
傷害、中毒および処置合併症	0	1 (3.2)	0	1 (1.6)	0
胃腸吻合部狭窄	0	1 (3.2)	0	1 (1.6)	0
臨床検査	1 (0.9)	0	0	0	0
肝酵素上昇	1 (0.9)	0	0	0	0
代謝および栄養障害	1 (0.9)	0	0	0	1 (1.6)
食欲減退	1 (0.9)	0	0	0	0
鉄欠乏	0	0	0	0	1 (1.6)
筋骨格系および結合組織障害	1 (0.9)	2 (6.5)	2 (6.1)	4 (6.3)	2 (3.3)
関節痛	0	1 (3.2)	2 (6.1)	3 (4.7)	1 (1.6)
背部痛	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

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TABLE 14.3__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term Among Non-randomized Subjects (SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
筋骨格系および結合組織障害 (Cont.)					
関節腫脹	0	1 (3.2)	0	1 (1.6)	0
筋肉痛	0	0	0	0	1 (1.6)
腎および尿路障害	1 (0.9)	0	0	0	2 (3.3)
高窒素血症	0	0	0	0	1 (1.6)
腎機能障害	1 (0.9)	0	0	0	0
排尿躊躇	0	0	0	0	1 (1.6)
生殖系および乳房障害	1 (0.9)	0	0	0	0
無月経	1 (0.9)	0	0	0	0
呼吸器、胸郭および縦隔障害	0	1 (3.2)	0	1 (1.6)	0
呼吸困難	0	1 (3.2)	0	1 (1.6)	0
皮膚および皮下組織障害	2 (1.9)	2 (6.5)	3 (9.1)	5 (7.8)	5 (8.2)
脱毛症	0	0	0	0	1 (1.6)
アレルギー性皮膚炎	0	0	0	0	1 (1.6)

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
皮膚および皮下組織障害 (Cont.)					
乾癬様皮膚炎	0	0	1 (3.0)	1 (1.6)	0
皮膚乾燥	1 (0.9)	0	0	0	0
湿疹	0	0	1 (3.0)	1 (1.6)	1 (1.6)
紅斑	0	0	1 (3.0)	1 (1.6)	0
そう痒症	0	0	0	0	1 (1.6)
乾癬	0	0	1 (3.0)	1 (1.6)	0
発疹	0	2 (6.5)	1 (3.0)	3 (4.7)	1 (1.6)
脂漏性皮膚炎	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

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表8

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STUDY M16-000 SUB-STUDY 1
R&D/21/0085 - CLINICAL/STATISTICAL
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TABLE 14.3__1.2.5.1

Subjects with Treatment-Emergent Severe Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
Any adverse event	11 (10.4)	3 (9.7)	2 (6.1)	5 (7.8)	4 (6.6)
血液およびリンパ系障害	1 (0.9)	0	0	0	0
貧血	1 (0.9)	0	0	0	0
胃腸障害	6 (5.7)	2 (6.5)	1 (3.0)	3 (4.7)	2 (3.3)
腹痛	0	0	1 (3.0)	1 (1.6)	0
クローン病	5 (4.7)	0	0	0	2 (3.3)
胃腸管瘻	1 (0.9)	0	0	0	0
胃腸の炎症	1 (0.9)	0	0	0	0
大腸閉塞	0	1 (3.2)	0	1 (1.6)	0
大腸穿孔	0	1 (3.2)	0	1 (1.6)	0
感染症および寄生虫症	2 (1.9)	0	0	0	0
腹部膿瘍	1 (0.9)	0	0	0	0
尿路感染	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__1.2.5.1

Subjects with Treatment-Emergent Severe Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
傷害、中毒および処置合併症	0	1 (3.2)	1 (3.0)	2 (3.1)	1 (1.6)
足関節部骨折	0	0	0	0	1 (1.6)
胃腸吻合部狭窄	0	1 (3.2)	0	1 (1.6)	0
処置による腸管穿孔	0	0	1 (3.0)	1 (1.6)	0
臨床検査	0	0	0	0	1 (1.6)
血中リン減少	0	0	0	0	1 (1.6)
代謝および栄養障害	1 (0.9)	0	0	0	0
低カリウム血症	1 (0.9)	0	0	0	0
精神障害	1 (0.9)	0	0	0	0
アルコール離脱症候群	1 (0.9)	0	0	0	0
血管障害	1 (0.9)	0	0	0	0
低血圧	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

表9

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KI MAB (CRO

STUDY M16-000 SUB-STUDY 1
R&D/21/0085 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 4

TABLE 14.3__2.2.1.1

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
Any adverse event	15 (14.2)	5 (16.1)	4 (12.1)	9 (14.1)	8 (13.1)
血液およびリンパ系障害	1 (0.9)	0	0	0	0
貧血	1 (0.9)	0	0	0	0
胃腸障害	9 (8.5)	4 (12.9)	2 (6.1)	6 (9.4)	4 (6.6)
腹痛	0	0	1 (3.0)	1 (1.6)	1 (1.6)
クローン病	7 (6.6)	2 (6.5)	1 (3.0)	3 (4.7)	2 (3.3)
腹膜垂炎	0	0	0	0	1 (1.6)
胃腸管瘻	1 (0.9)	0	0	0	0
胃腸の炎症	1 (0.9)	0	0	0	0
腸管狭窄	0	0	0	0	1 (1.6)
大腸閉塞	0	1 (3.2)	0	1 (1.6)	0
大腸穿孔	0	1 (3.2)	0	1 (1.6)	0
直腸炎	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__2.2.1.1

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
肝胆道系障害	1 (0.9)	0	0	0	0
胆石症	1 (0.9)	0	0	0	0
感染症および寄生虫症	3 (2.8)	0	1 (3.0)	1 (1.6)	0
腹部膿瘍	1 (0.9)	0	0	0	0
ウイルス性気管支炎	0	0	1 (3.0)	1 (1.6)	0
クロストリジウム・ディフィシレ感染	1 (0.9)	0	0	0	0
胃腸炎	1 (0.9)	0	0	0	0
肺炎	1 (0.9)	0	0	0	0
傷害、中毒および処置合併症	0	1 (3.2)	1 (3.0)	2 (3.1)	1 (1.6)
足関節部骨折	0	0	0	0	1 (1.6)
胃腸吻合部狭窄	0	1 (3.2)	0	1 (1.6)	0
処置による腸管穿孔	0	0	1 (3.0)	1 (1.6)	0
代謝および栄養障害	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__2.2.1.1

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
代謝および栄養障害 (Cont.)					
低カリウム血症	1 (0.9)	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0	1 (1.6)
関節障害	0	0	0	0	1 (1.6)
神経系障害	0	1 (3.2)	0	1 (1.6)	0
痙攣発作	0	1 (3.2)	0	1 (1.6)	0
精神障害	1 (0.9)	0	0	0	0
アルコール離脱症候群	1 (0.9)	0	0	0	0
腎および尿路障害	0	0	0	0	1 (1.6)
高窒素血症	0	0	0	0	1 (1.6)
尿路結石	0	0	0	0	1 (1.6)
呼吸器、胸郭および縦隔障害	0	0	0	0	1 (1.6)
肺塞栓症	0	0	0	0	1 (1.6)
血管障害	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

TABLE 14.3__2.2.1.1

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
血管障害 (Cont.)					
低血圧	1 (0.9)	0	0	0	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

表10

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KI MAB (CRO
STUDY M16-000 SUB-STUDY 1
R&D/21/0085 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.2.3.1

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation
of Study Drug by System Organ Class and Preferred Term
Among Non-randomized Subjects
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo SC (N=106) n (%)	Risankizumab 180 mg SC (N=31) n (%)	Risankizumab 360 mg SC (N=33) n (%)	Risankizumab Total (N=64) n (%)	Risankizumab Rescue Therapy* (N=61) n (%)
Any adverse event	5 (4.7)	1 (3.2)	0	1 (1.6)	1 (1.6)
胃腸障害	5 (4.7)	0	0	0	1 (1.6)
クローン病	4 (3.8)	0	0	0	1 (1.6)
胃腸管瘻	1 (0.9)	0	0	0	0
胃腸の炎症	1 (0.9)	0	0	0	0
感染症および寄生虫症	1 (0.9)	0	0	0	0
腹部膿瘍	1 (0.9)	0	0	0	0
筋骨格系および結合組織障害	0	1 (3.2)	0	1 (1.6)	0
関節腫脹	0	1 (3.2)	0	1 (1.6)	0
呼吸器、胸郭および縦隔障害	0	1 (3.2)	0	1 (1.6)	0
呼吸困難	0	1 (3.2)	0	1 (1.6)	0

Note: Treatment emergent AEs (TEAEs) for M16-000 sub-study 1 are defined as events that begin either on or after the first dose of the study drug in the sub-study 1 and within 140 days after the last dose administration of the study drug in the sub-study 1 for subjects who do not participate in the sub-study 3 or until first dose of study drug in the sub-study 3 if the subject is enrolled into the sub-study 3.
SA1 Population includes all subjects who received at least one dose of study drug in the sub-study 1.
Subjects are counted once in each row, regardless of the number of events they may have had.
* Risankizumab rescue therapy is one dose of open-label 1200 mg IV followed by 360 mg SC through the end of the sub-study 1. All events happened after receiving risankizumab rescue therapy regardless the previous treatments are presented in this column. AEs happened before receiving risankizumab rescue therapy will be presented in their original treatment group.

Program Source Code: [redacted]

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
血中アルカリホスファターゼ増加				X
脂肪肝				X
肝腫大				X
小腸閉塞	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
DIABETES MELLITUS: TYPE 2	19[redacted]
OTHER: POST MENAPAUSAL	20[redacted]
OSTEOARTHRITIS	20[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPERLIPIDEMIA: N/A	20[redacted]
CORONARY ARTERY DISEASE: N/A	20[redacted]
HYPERTENSION	20[redacted]
OTHER: DIVERTICULOSIS	20[redacted]
OTHER: PERIPHERAL NEUROPATHY	20[redacted]
CROHN'S DISEASE	20[redacted]
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: C-SECTION	19[redacted]
SURGERY: CAESAREAN SECTION	19[redacted]
SURGERY: UMBILICAL HERNIA	19[redacted]
SURGERY: UMBILICAL HERNIA REPAIR	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
SURGERY: CAROTID ENDARTECTOMY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 34	[redacted]20[redacted] / 34	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 120	[redacted]20[redacted] / 120	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 148	[redacted]20[redacted] / 148	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 148	[redacted]20[redacted] / 148	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 176	[redacted]20[redacted] / 176	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 236	[redacted]20[redacted] / 236	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 285	[redacted]20[redacted] / 285	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 344	[redacted]20[redacted] / 344	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 397	[redacted]20[redacted] / 397	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 453	[redacted]20[redacted] / 453	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 517	[redacted]20[redacted] / 517	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
DULOXETINE	30 mg	QD	Y-M: 20[redacted]
LISINOPRIL	20 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	108 mg	EVERY WEEK	Y-M: 20[redacted]
CERTOLIZUMAB	400 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
CERTOLIZUMAB	400 mg	OTHER: WEEKS 0, 2, AND 4	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]

CERTOLIZUMAB	400 mg	QM	Y-M: 20[redacted]
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: WK 0, 2, AND 6	Y-M: 20[redacted]
VEDOLIZUMAB	108 mg	EVERY WEEK	Y-M: 20[redacted]
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted]
GLIMEPIRIDE	6 mg	QD	Y-M: 20[redacted]
IRON	324 mg	QD	Y-M: 20[redacted]
CYANOCOBALAMIN	3000 ug	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	50000 IU	QD	Y-M: 20[redacted]
COLESTIPOL	1 g	TID	Y-M: 20[redacted] / -240
UBIDECARENONE	100 mg	QD	Y-M: 20[redacted] / -179
METFORMIN	1000 mg	BID	Y-M: 20[redacted] / -87
PICO-SALAX	5 OTHER: OZ	OTHER: ONCE	Y-M: 20[redacted] / -11
FENTANYL	2 ug	OTHER: ONCE	Y-M: 20[redacted] / -10
MIDAZOLAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / -10
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / -10
PROPOFOL	300 mg	OTHER: ONCE	Y-M: 20[redacted] / -10
AMITRIPTYLINE	50 mg	QD	Y-M: 20[redacted] / 21
FLUTICASONE	2 OTHER: SPRAYS	BID	Y-M: 20[redacted] / 53
FLUTICASONE	50 ug	PRN	Y-M: 20[redacted] / 53
AMITRIPTYLINE	50 mg	QD	Y-M: 20[redacted] / 82
AZELASTINE	205.5 ug	QD	Y-M: 20[redacted] / 82
PICO-SALAX	5 OTHER: OZ	OTHER: ONCE	Y-M: 20[redacted] / 82
PROPOFOL	300 mg	OTHER: ONCE	Y-M: 20[redacted] / 83
GABAPENTIN	300 mg	QD	Y-M: 20[redacted] / 162
CETIRIZINE	10 mg	QD	Y-M: 20[redacted] / 174

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	10 mg	QD	Y-M: 20[redacted]	NOT REPORTED
COLESTIPOL	1 g	TID	Y-M: 20[redacted] / -240	NOT REPORTED
FLUTICASONE	2 OTHER: SPRAYS	BID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 186
AZELASTINE	205.5 ug	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 217
GABAPENTIN	300 mg	QD	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 376
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 181

INSULIN LISPRO	6 IU	PRN	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 182
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 182
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 181	Y-M: 20[redacted] / 182
PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 371	ONGOING
CANNABIS SATIVA	500 mg	QD	Y-M: 20[redacted] / 447	Y-M: 20[redacted] / 449
CYANOCOBALAMIN	1000 ug	QD	Y-M: 20[redacted] / 453	NOT REPORTED
CYANOCOBALAMIN	1000 ug	QD	Y-M: 20[redacted] / 453	ONGOING
THIOCTIC ACID	600 mg	QD	Y-M: 20[redacted] / 520	ONGOING
FLUCONAZOLE	150 mg	OTHER: ONCE	Y-M: 20[redacted] / 554	Y-M: 20[redacted] / 554
CLOBETASOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 572	Y-M: 20[redacted] / 583
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted] / 845	ONGOING
EXENATIDE	2 mg	OTHER: WEEKLY	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 888
INSULIN GLARGINE	5 OTHER: UNITS	PRN	Y-M: 20[redacted] / 901	ONGOING

Event #1: Serious Adverse Event

Event Description	PARTIAL SMALL BOWEL OBSTRUCTION
Preferred Term	小腸閉塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 180
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 180): Glucose: 15.3 [3.9 - 6.1] MMOL/L; Leukocytes: 11.9 [4.5 - 11] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 182): CT ABDOMINAL/PELVIS WITH CONTRAST:SMALL BOWEL OBSTRUCTION

AE Stopped Rx Day	182
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DISEASE UNDER STUDY
Discontinued Study Drug Due to the Event	NO

SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Hepatic Events

Event Description	HEPATIC STEATOSIS, HEPATOMEGLY, ELEVATED ALKALINE PHOSPHATASE
Preferred Term	血中アルカリホスファターゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 365
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #3: Event of Interest - Hepatic Events

Event Description	HEPATIC STEATOSIS, HEPATOMEGLY, ELEVATED ALKALINE PHOSPHATASE
Preferred Term	脂肪肝
AE Onset Date / Rx Day	[redacted]20[redacted] / 365
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Event of Interest - Hepatic Events

Event Description	HEPATIC STEATOSIS, HEPATOMEGLY, ELEVATED ALKALINE PHOSPHATASE
Preferred Term	肝腫大
AE Onset Date / Rx Day	[redacted]20[redacted] / 365
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:09:28
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

米国の治験責任医師からの報告。本被験者は 6[redacted] 歳女性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，部分的な小腸閉塞の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，帝王切開手術，臍ヘルニア，2 型糖尿病，閉経後症状，臍ヘルニア修復手術，胃食道逆流性疾患，高脂血症，冠動脈疾患，憩室症，高血圧，クローン病，鉄欠乏性貧血，非喫煙者及び非飲酒者であった。

被験者は，20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで先行試験 M16-006 に組み入れられ，盲検化された治験薬が投与された。

投与 180 日後，被験者は部分的な小腸閉塞を発現した。投与 182 日後，部分的な小腸閉塞は消失した。

投与 180 日後，被験者は早朝から重度の腹痛があったため，救急治療室を受診した。悪心及び嘔吐もあった。腹部 CT 検査が行われ，部分的な小腸閉塞が確認された。被験者は，経鼻胃管が留置されて絶食となり，入院した。被験者の症状は消失し，経鼻胃管は抜去された。軟食が開始され，被験者はよく摂取できていた。投与 182 日後，被験者は，安定した状態で退院した。

投与された薬剤は，Protonix，モルヒネ，アセトアミノフェン及び Zofran であった。

The patient's past medications include:

VEDOLIZUMAB for CROHN'S DISEASE ([redacted])

CERTOLIZUMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Partial small intestinal obstruction (10056357) (Small intestinal obstruction (10041101)) [v.23.0] [10056357]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of PARTIAL SMALL BOWEL OBSTRUCTION

- Investigator: DISEASE UNDER STUDY

- AbbVie: Event more likely related to pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20**[redacted] **BLOOD GLUCOSE:** 275 mg/dL (normal 70 to 110)

[redacted] 20[redacted] CT ABDOMEN PELVIS: small bowel obstruction

[redacted] **20**[redacted] **WBC:** 11.9 X10**3/MCL (normal 4.5 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
尿管結石症	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: TONSILLITIS	19[redacted]
CROHN'S DISEASE	19
GASTROESOPHAGEAL REFLUX DISEASE	19
OTHER: DEGENERATIVE JOINT DISEASE	19
OSTEOARTHRITIS	20
OTHER: INSOMNIA	20
NEPHROLITHIASIS	20
HYPERTENSION	20
OTHER: HIATAL HERNIA	20
DEPRESSION: DEPRESSION	20
CHOLECYSTITIS	20
OTHER: SMALL BOWEL OBSTRUCTION	20
OTHER: ANXIETY	20
LIVER DISEASE (EXCLUDING HEPATITIS): FATTY LIVER	20
OTHER: DIVERTICULOSIS	20
KIDNEY DISORDER: BI-LATERAL RENAL CYSTS	20
OTHER: B-12 DEFICIENCY	20

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	19[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	19
SURGERY: PARTIAL COLECTOMY	19
SURGERY: SMALL BOWEL RESECTION	19
SURGERY: LEFT KNEE REPLACEMENT	19
SURGERY: CHOLECYSTECTOMY	20
CROHN'S DISEASE HISTORY: COLONOSCOPY	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	5 CIGARETTE	40	
CIGARS	NEVER			
E-CIGARETTES	NEVER			

PIPES NEVER

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 114	[redacted]20[redacted] / 114	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 142	[redacted]20[redacted] / 142	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 142	[redacted]20[redacted] / 142	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 176	[redacted]20[redacted] / 176	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 176	[redacted]20[redacted] / 176	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 232	[redacted]20[redacted] / 232	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 232	[redacted]20[redacted] / 232	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 302	[redacted]20[redacted] / 302	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 302	[redacted]20[redacted] / 302	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 344	[redacted]20[redacted] / 344	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 344	[redacted]20[redacted] / 344	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 400	[redacted]20[redacted] / 400	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 400	[redacted]20[redacted] / 400	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 456	[redacted]20[redacted] / 456	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 456	[redacted]20[redacted] / 456	1

PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 512	[redacted]20[redacted] / 512	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 512	[redacted]20[redacted] / 512	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
LOPERAMIDE	2 OTHER: CAPLETS	QD	Y-M: 20[redacted]
ALPRAZOLAM	0.5 mg	BID	Y-M: 20[redacted]
LISINOPRIL	5 mg	QD	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
LOPERAMIDE	2 OTHER: CAPLETS	QD	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 424
ALPRAZOLAM	0.5 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 728
LISINOPRIL	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
KETOROLAC	30 mg	PRN	Y-M: 20[redacted]-[redacted] / 424	Y-M: 20[redacted]-[redacted] / 425
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted]-[redacted] / 424	Y-M: 20[redacted]-[redacted] / 425
MORPHINE	4 mg	PRN	Y-M: 20[redacted]-[redacted] / 424	Y-M: 20[redacted]-[redacted] / 426
LOPERAMIDE	2 OTHER: CAPS	PRN	Y-M: 20[redacted]-[redacted] / 425	ONGOING
VICODIN	5/325 mg	PRN	Y-M: 20[redacted]-[redacted] / 425	Y-M: 20[redacted]-[redacted] / 454

Event #1: Serious Adverse Event

Event Description RIGHT URETERAL CALCULUS
Preferred Term 尿管結石症
AE Onset Date / Rx Day [redacted]20[redacted] / 424
Age at AE Onset 6[redacted]
Laboratory Testing
[redacted]20[redacted] (Rx Day 425): NPTST541-URINALYSIS W/REFLEX: NORMAL [NOT REPORTED - NOT REPORTED] DIPSTICK
Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 424): CT OF THE ABDOMEN/PELVIS:RIGHT URETERAL CALCULUS WITH OBSTRUCTION; [redacted]20[redacted] (Rx Day 425): CYSTOSCOPY:RIGHT URETERAL CALCULUS; TELEMETRY MONITOR:NORMAL SINUS RHYTHM, BRADYCARDIA; URETERAL STENT PLACEMENT:RIGHT URETERAL CALCULUS

AE Stopped Rx Day	426
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	H/O KIDNEY STONES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:09:28
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

米国の治験責任医師からの報告。本被験者は6[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，右尿管結石の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，胃食道逆流性疾患，変形性関節症，腎結石症，高血圧，胆嚢炎，両側腎嚢胞，喫煙者（1 日 5 本を 40 年間）及び飲酒者（1 日 2 杯未満）であった。

投与 424 日後，被験者は右尿管結石を発現した。投与 426 日後，右尿管結石は消失した。

投与 424 日後，被験者は急性の腹痛及び右側腹部痛（鋭い痛みで重症度は中等度）のため入院した。同日，CT スキャン検査の結果，5 mm の右尿管結石による閉塞に続発する右尿管水腎症が明らかになった。泌尿器科医による診察となり，膀胱鏡検査及び尿管ステント留置が行われた。膀胱鏡検査後，被験者は徐脈（40 ～60 bpm，非重篤）を発現し，テレメトリーが開始された。循環器専門医による診察が行われ，循環器専門医の見地から，被験者の状態は安定しており，退院は可能と判断された。投与 426 日後，被験者は，安定した状態で退院し，循環器専門医及び泌尿器科医による経過観察が行われることとなった。

被験者は，これより前の 20[redacted] 年に尿管ステントによる腎結石を発現していた。

投与された薬剤は，Zofran，Norco，Toradol 及びモルヒネであった。

Causality for RISANKIZUMAB (Blinded)

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1) Ureteral calculus (10046383) (Ureterolithiasis (10077989)) [v.23.0] [10046383]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of RIGHT URETERAL CALCULUS

- Investigator: History of kidney stones

- AbbVie: event is more likely related to pre-existing history of nephrolithiasis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT SCAN:** abdominal/pelvis: Right hydroureteronephrosis, secondary to an obstructing 5 mm right ureteral calculus; additional non-obstructing calculus were noted measuring from 3 to 1 mm in size. There is also a non-obstructing 2 mm calculus in the left kidney. Right renal cyst measures up to 7.5 cm.

[redacted] **20[redacted] CYSTOSCOPY:** right ureteral calculus

[redacted] **20[redacted] TELEMETRY MONITOR:** normal sinus rhythm, bradycardia - HR was 60 bpm

[redacted] 20[redacted] URINALYSIS: dipstick - 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
ＨＥＲ２陽性乳癌	X	X		X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	4[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
CROHN'S DISEASE	19[redacted]
OTHER: HEMORRHOIDS	20[redacted]
OTHER: UTERINE FIBROIDS	20[redacted]
OTHER: GASTRITIS	20[redacted]
TUBERCULOSIS: LATENT TB. WAS ON IZONIIAZIDE	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: ILEAL RESECTION	19[redacted]
SURGERY: TUBAL LIGATION	20[redacted]
SURGERY: HYSTERECTOMY	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 33	[redacted]20[redacted] / 33	1

M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 33	[redacted]20[redacted] / 33	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 97	[redacted]20[redacted] / 97	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 156	[redacted]20[redacted] / 156	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 187	[redacted]20[redacted] / 187	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 261	[redacted]20[redacted] / 261	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 323	[redacted]20[redacted] / 323	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 372	[redacted]20[redacted] / 372	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 449	[redacted]20[redacted] / 449	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ISONIAZID	300 mg	QD	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
MAALOX	20 mL	PRN	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 454
INFLUENZA VACCINE	60 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 586	Y-M: 20[redacted] / 586
ERGOCALCIFEROL	5000 IU	QD	Y-M: 20[redacted] / 630	ONGOING
IRON	325 mg	QD	Y-M: 20[redacted] / 630	ONGOING
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 630	ONGOING
VACCINIUM MACROCARPON	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 630	ONGOING
LORAZEPAM	0.5 mg	OTHER: TID PRN	Y-M: 20[redacted] / 632	ONGOING
ONDANSETRON	4 mg	OTHER: TID PRN	Y-M: 20[redacted] / 635	ONGOING
DEXAMETHASONE	8 mg	OTHER: Q WEEKLY	Y-M: 20[redacted] / 638	ONGOING

DIPHENHYDRAMINE	25 mg	OTHER: Q WEEKLY	Y-M: 20[redacted] / 638	ONGOING
FAMOTIDINE	20 mg	OTHER: Q WEEKLY	Y-M: 20[redacted] / 638	ONGOING
PACLITAXEL	WEEKLY FOR 11 WEEKS OTHER: VARIABLE DOSING	OTHER: WEEKLY FOR 11 WEEKS	Y-M: 20[redacted] / 638	Y-M: 20[redacted] / 716
TRASTUZUMAB	EVERY 3 WEEKS FOR 12 WEEKS OTHER: VARIABLE DOSING	OTHER: EVERY 3 WEEKS FOR 12 WEEKS	Y-M: 20[redacted] / 638	Y-M: 20[redacted] / 716
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: WIG	PRN	Y-M: 20[redacted] / 653	ONGOING
EMLA	2.5/2.5 %	QD	Y-M: 20[redacted] / 654	ONGOING
LOPERAMIDE	2 OTHER: CAPLETS	PRN	Y-M: 20[redacted] / 654	ONGOING
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 654	ONGOING
PROCHLORPERAZINE	10 mg	TID	Y-M: 20[redacted] / 654	ONGOING
PARACETAMOL	650 mg	OTHER: ONCE	Y-M: 20[redacted] / 666	Y-M: 20[redacted] / 666
CLINDAMYCIN	1 %	BID	Y-M: 20[redacted] / 695	ONGOING

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

Event Description POSITIVE HER 2 LEFT BREAST CANCER

Preferred Term ＨＥＲ２陽性乳癌

AE Onset Date / Rx Day [redacted]20[redacted] / 311

Age at AE Onset 4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (Rx Day 587): OTHER BREAST TISSUE ER ESTROGEN RECEPTOR: Positive-95% STRONG INTENSITY POSITIVE; OTHER BREAST TISSUE HER-2: Positive-3+ POSITIVE; OTHER BREAST TISSUE MIB-1 (KI-67): Positive-64% HIGH; OTHER BREAST TISSUE P53: Positive-41% POSITIVE; OTHER BREAST TISSUE PR PROGESTERONE RECEPTOR: Positive-95% STORNG INTENSITY POSITIVE

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 317): BREAST ULTRASOUND:NO ABNORMALITIES FOUND AT THAT TIME; [redacted]20[redacted] (Rx Day 502): REPEAT MAMMOGRAM:ABNORMAL FINDINGS STILL SEEN IN BREAST;SUBCENTIMETER NODULAR ASYMMETRIES IN THE OUTER HEMISPHERE

POSTERIORLY ARE STABLE -- IMPRESSION: STABLE PROBABLY BENIGN FINDINGS; [redacted]20[redacted] (Rx Day 531): BILATERAL MRI SCAN OF BOTH BREASTS WITH AND WITHOUT INTRAVENOUS CONTRAST:IN THE 6:00 POSITION OF THE LEFT BREAST THERE IS AN 8 X 7 MM IRREGULAR ENHANCING NODULE WITH SUSPICIOUS ENHANCEMENT CHARACTERISTICS POORLY DEFINED MARGINS. NO FOCALLY SUSPICIOUS AREAS OF ENHANCEMENT; [redacted]20[redacted] (Rx Day 581): SECOND LOOK ULTRASOUND LEFT BREAST:REVEALED 8X6X7MM SPICULATED NODULE AT THE 6:30 TO 7:00 O'CLOCK POSITION, 4 CM FROM THE NIPPLE 6 MM HYPOCHOIC STRUCTURE AT THE 2 O'CLOCK POSITION, 4 CM FROM THE NIPPLE, RIGHT SIDE REVEALED A COMPLEX CY; [redacted]20[redacted] (Rx Day 587): BREAST ULTRASOUND WITH NEEDLE BIOPSY:LEFT BREAST AT 6:30 VIA ULTRASOUND-GUIDED CORE BIOPSY FINDINGS WERE INFILTRATING POORLY DIFFERENTIATED DUCTAL CARCINOMA. LEFT BREAST AT 2 O'CLOCK, FINE NEEDLE ASPIRATION WITH FINDINGS OF SCATTERED BE; [redacted]20[redacted] (Rx Day 608): ULTRASOUND LEFT BREAST:LEFT AXILLA GUIDED CORE BIOPSY FRAGMENTS OF BENIGN LYMPH TISSUE; [redacted]20[redacted] (Rx Day 618): LUMPECTOMY AND REMOVAL OF 3 LYMPH NODES; MEDICATION PORT INSTALLED:LEFT BREAST LUMPEDTOMY: INVASIVE DUCTAL CARCINOMA, POORLY DIFFERENTIATED, 7MM; DUCTAL CARCINOMA IN SITU (DCIS), SOLID AND CRIBRIFORM TYPES WITH HIGH NUCLEAR GRADE AND NECROSIS; DCIS IS EXTENSIVE, PRES; LUMPECTOMY AND REMOVAL OF 3 LYMPH NODES; MEDICATION PORT INSTALLED (CONT'D):LUMPECTOMY:SENTINEL LYMPH NODE SAMPLING, SINGLE FOCUS OF INVASIVE CARCINOMA (7MM) DUCTAL GRADE 3/3 8/9 POINTS TUBAL FORMATION, <10% TUBULES; VESTICULAR NUCLEI WITH PROMINENT NUCLEOLI AND MARKED VARIAT

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ENVIRONMENTAL FACTORS AND CHANCE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:09:28
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

米国の治験責任医師からの報告。本被験者は4[redacted]歳女性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，HER2 陽性左乳癌の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，非喫煙者及び飲酒者（1 日 2～4 杯）であった。

投与 311 日後，被験者は HER2 陽性左乳癌を発現した。

投与から約 10 ヵ月後，婦人科健診で乳房腫瘤が認められた。投与から約 10 ヵ月後 20[redacted] 年[redacted] 月，乳房超音波検査が実施され，投与から約 16 ヵ月後，重ねて乳房撮影が実施された。両検査で，悪性の疑いは否定された。医師は，MRI 検査を強く推奨した。投与 531 日後，両側乳房の追加 MRI 検査が実施され，左乳房下部に 8×7 mm の小結節が認められた。投与 587 日後，超音波ガイド下コア生検を伴うセカンドルック超音波検査が行われ，浸潤性の低分化型乳管癌が明らかになった。5 つの病理診断の結果は，様々な解釈の結果と報告された。

投与 618 日後，左乳房乳腺腫瘤摘出術及び 3 つのリンパ節の切除が行われた。その結果，充実性や篩状の形態を示す 7 mm の低分化型 HER2 陽性腺管上皮内癌（DCIS）が明らかになり，高度の核異型及び壊死を伴っていた。薬剤投与用のポートも設置された。

治験薬の投与は完全に中止された。

投与された薬剤は，ハーセプチン及びタキソールであった。

Causality for RISANKIZUMAB (Blinded)

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1) HER2 positive breast cancer (10065430) (HER2 positive breast cancer (10065430)) [v.23.1] [10065430]

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

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

Dechallenge: No

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of POSITIVE HER 2 LEFT BREAST CANCER

- Investigator: Environmental factors and chance.

- AbbVie: Weak temporal relationship since breast lesions were first known to be present within 10 months of study drug exposure (includes both prior protocol exposure and current protocol exposure). In addition, published literature indicates that inhibition of IL-23 is unlikely to increase the risk for cancer. Expression of IL-23 is increased in human tumors. Preclinical data have, moreover, demonstrated beneficial effect of IL-23 p19 inhibition in animal models, both for pre-existing and tumor-induction models (Langowski. Nature 20[redacted]).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BILATERAL MRI SCAN OF BOTH BREASTS WITH AND WITHOUT INTRAVENOUS CONTRAST:** IN THE 6:00 POSITION OF THE LEFT BREAST THERE IS AN 8 x 7 mm IRREGULAR ENHANCING NODULE WITH SUSPICIOUS ENHANCEMENT CHARACTERISTICS POORLY DEFINED MARGINS. NO FOCALLY SUSPICIOUS AREAS OF ENHANCEMENT IN THE RIGHT BREAST TO SUGGEST MALIGNANCY.

[redacted] **20[redacted] BREAST ULTRASOUND:** NEGATIVE FOR SUSPECTED MALIGNANCIES

[redacted] **20[redacted] BREAST ULTRASOUND WITH NEEDLE BIOPSY:** LEFT BREAST AT 6:30 VIA ULTRASOUND-GUIDED CORE BIOPSY FINDINGS WERE INFILTRATING POORLY DIFFERENTIATED DUCTAL CARCINOMA. LEFT BREAST AT 2 O'CLOCK, FINE NEEDLE ASPIRATION WITH FINDINGS OF SCATTERED BENIGN-APPEARING DUCTAL CELLS IN A BACKGROUND OF DEGENERATED CELLS AND DEBRIS SUGGESTIVE OF BENIGN CYST.

[redacted] **20[redacted] ER ESTROGEN RECEPTOR:** BREAST TISSUE: 95% STRONG INTENSITY POSITIVE

[redacted] **20[redacted] HER-2:** BREAST TISSUE: 3+ POSITIVE

20[redacted] HISTOLOGY: DCIS is extensive, present on 8 of 12 histologically examined slides, spanning approx. 24 mm; no lymphovascular invasion identified; margins with invasive carcinoma, anterior 2 mm, all remaining >10 mm; DCIS anterior 2 mm, superior 2.5 mm, lateral 5 mm all remaining >10 mm; biopsy site changes are present; 2 lymph notes; negative for metastatic carcinoma (0/2).

[redacted] **20[redacted] MAMMOGRAM:** NEGATIVE FOR SUSPECTED MALIGNANCIES

[redacted] **20[redacted] MIB-1 (KI-67):** BREAST TISSUE: Positive, 64% HIGH

[redacted] **20[redacted] P53:** BREAST TISSUE: 41% POSITIVE

[redacted] **20[redacted] PATHOLOGY:** Sentinel lymph node sampling, single focus of invasive carcinoma (7mm) ductal grade 3/3 8/9 points tubal formation, <10% tubules; vesticular nuclei with prominent nucleoli and marked variation, mitotic rate score 2: 4-7 mitoses/ mm2 Cuctal carcinoma in-situ: EIC positive; 2 sentinel lymph nodes present, 0 sentinel lymph nodes positive for macrometastasses,2 non-sentinel lymph nodes present with 0 positive for micrometastasses Pathologic classifications : pT1b, pIVO; HER-2 positive breast cancer.

[redacted] **20[redacted] PR PROGESTERONE RECEPTOR:** BREAST TISSUE: 95% STORNG INTENSITY POSITIVE

[redacted] **20[redacted] SECOND LOOK ULTRASOUND LEFT BREAST:** REVEALED 8X6X7MM SPICULATED NODULE AT THE 6:30 TO 7:00 O'CLOCK POSITION, 4 CM FROM THE NIPPLE 6 MM HYPOCHOIC STRUCTURE AT THE 2 O'CLOCK POSITION, 4 CM FROM THE NIPPLE, RIGHT SIDE REVEALED A COMPLEX CYST AND AN INTRMAMMMARY LYMPH NODE, ALL STABLE

[redacted] **20[redacted] ULTRASOUND LEFT BREAST:** LEFT AXILLA GUIDED CORE BIOPSY FRAGMENTS OF BENIGN LYMPH TISSUE

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
冠動脈疾患				X
痙攣発作	X			
ストレス心筋症				X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	7[redacted]	MALE	WHITE

Medical History	Onset Year
HYPERTENSION	20[redacted]
CROHN'S DISEASE	20
DEPRESSION: CONTROLLED WITH MEDICATION	20
OSTEOARTHRITIS	20
OTHER: ANXIETY	20
MIGRAINE HEADACHE	20
GASTROESOPHAGEAL REFLUX DISEASE	20
ANEMIA: PERNICIOUS ANEMIA	20
OTHER: OBSESSIVE COMPULSIVE DISORDER	20
CARDIAC ARRHYTHMIA: ATRIAL FLUTTER	20
OTHER: HEART MURMUR	20
CARDIAC ARRHYTHMIA: ATRIAL FIBRILLATION	20
OTHER: HYPOKALEMIA	20

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	10 CIGARETTE	7	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 58	[redacted]20[redacted] / 58	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 58	[redacted]20[redacted] / 58	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 99	[redacted]20[redacted] / 99	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 114	[redacted]20[redacted] / 114	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 143	[redacted]20[redacted] / 143	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 143	[redacted]20[redacted] / 143	1
M16006 /RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 143	[redacted]20[redacted] / 143	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 185	[redacted]20[redacted] / 185	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 185	[redacted]20[redacted] / 185	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 241	[redacted]20[redacted] / 241	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 241	[redacted]20[redacted] / 241	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 297	[redacted]20[redacted] / 297	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 297	[redacted]20[redacted] / 297	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 361	[redacted]20[redacted] / 361	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 361	[redacted]20[redacted] / 361	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 409	[redacted]20[redacted] / 409	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 409	[redacted]20[redacted] / 409	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 464	[redacted]20[redacted] / 464	1

RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 464 464	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 521 521	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 521 521	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ALPRAZOLAM	1 mg	TID	Y-M: 20[redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]
FOLIC ACID	800 ug	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	OTHER: 1 X PER WEEK	Y-M: 20[redacted]
FISH OIL	1200 mg	QD	Y-M: 20[redacted]
IBUPROFEN	400 mg	PRN	Y-M: 20[redacted]
CITALOPRAM	20 mg	QD	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted]
TILACTASE	1 OTHER: TABLET	PRN	Y-M: 20[redacted]
LOSARTAN	100 mg	QD	Y-M: 20[redacted] / -295
PRAZOSIN	2 mg	QD	Y-M: 20[redacted] / -295
METOPROLOL	25 mg	QD	Y-M: 20[redacted] / -224
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted] / -139
WARFARIN	5 mg	OTHER: FOUR TIMES PER WEEK (T, TH, SAT, SUN)	Y-M: 20[redacted] / -81
WARFARIN	7.5 mg	OTHER: THREE TIMES PER WEEK (M, W, F)	Y-M: 20[redacted] / -81
POTASSIUM	20 mEq	BID	Y-M: 20[redacted] / 32
KETOCONAZOLE	2 OTHER: %	BID	Y-M: 20[redacted] / 168

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	800 ug	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 482
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 482
TILACTASE	1 OTHER: TABLET	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 482
PRAZOSIN	2 mg	QD	Y-M: 20[redacted] / -295	Y-M: 20[redacted] / 482
CYANOCOBALAMIN	1000 ug	OTHER: Q 30 DAYS	Y-M: 20[redacted] / 302	NOT REPORTED

PREDNISOLONE	1 %	QID	Y-M: 20[redacted] / 471	Y-M: 20[redacted] / 518
ALPRAZOLAM	1 mg	BID	Y-M: 20[redacted] / 480	NOT REPORTED
OLANZAPINE	5 mg	QID	Y-M: 20[redacted] / 482	NOT REPORTED
PROMETHAZINE	6.25 mg	PRN	Y-M: 20[redacted] / 482	NOT REPORTED
IOHEXOL	100 mL	OTHER: ONCE	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 482
MAGNESIUM SULFATE	3 g	OTHER: ONCE	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 482
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 482
PARACETAMOL	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 482
PHYTOMENADIONE	5 mg	BID	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 482
PLASMA	2 OTHER: UNITS	OTHER: ONCW	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 482
POTASSIUM	60 mEq	OTHER: ONCE	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 482
VANCOMYCIN	1750 mg	OTHER: ONCE	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 482
LEVETIRACETAM	500 mg	BID	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 483
LIDOCAINE	1 OTHER: MG/MIN	OTHER: CONTINUOUS	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 483
SODIUM CHLORIDE	1000 mL	PRN	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 483
AMPICILLIN	2000 mg	OTHER: Q 4 HOURS	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 484
CEFTRIAXONE	2000 mg	BID	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 484
VANCOMYCIN	1250 mg	BID	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 484
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 486
ACETYLSALICYLIC ACID	325 mg	OTHER: ONCE	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 487
LORAZEPAM	1 mg	PRN	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 488
POTASSIUM	40 mEq	OTHER: Q 6 HOURS	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 490
MELATONIN	3 mg	QD	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 492
SODIUM CHLORIDE	25 mL	PRN	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 492

POTASSIUM	40 mEq	QD	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 493
FOSPHENYTOIN	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 483	Y-M: 20[redacted] / 483
LEVETIRACETAM	1000 mg	BID	Y-M: 20[redacted] / 483	Y-M: 20[redacted] / 484
LISINOPRIL	5 mg	QD	Y-M: 20[redacted] / 483	Y-M: 20[redacted] / 485
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / 484	NOT REPORTED
COMBIVENT	3 mL	PRN	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 484
FOSPHENYTOIN	200 mg	BID	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 484
FOSPHENYTOIN	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 484
FUROSEMIDE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 484
VANCOMYCIN	1500 mg	BID	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 484
HEPARIN	5000 OTHER: UNITS	BID	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 486
FENTANYL	25 ug	PRN	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 491
LEVETIRACETAM	1500 mg	BID	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 492
WARFARIN	7.5 mg	QD	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 492
AMIODARONE	200 mg	QD	Y-M: 20[redacted] / 485	Y-M: 20[redacted] / 486
CEFTRIAXONE	2000 mg	QD	Y-M: 20[redacted] / 485	Y-M: 20[redacted] / 491
HEPARIN	2000 OTHER: UNITS	OTHER: ONCE	Y-M: 20[redacted] / 486	Y-M: 20[redacted] / 486
AMIODARONE	1.8 OTHER: MG/ML	OTHER: CONTINUOUS	Y-M: 20[redacted] / 486	Y-M: 20[redacted] / 488
LISINOPRIL	10 mg	QD	Y-M: 20[redacted] / 486	Y-M: 20[redacted] / 491
DIGOXIN	500 ug	QD	Y-M: 20[redacted] / 487	Y-M: 20[redacted] / 488
CARVEDILOL	3.125 mg	BID	Y-M: 20[redacted] / 488	Y-M: 20[redacted] / 489
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 488	Y-M: 20[redacted] / 493
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / 490	Y-M: 20[redacted] / 490
CARVEDILOL	6.25 mg	BID	Y-M: 20[redacted] / 490	Y-M: 20[redacted] / 491

PROPOFOL	120 mg	OTHER: ONCE	Y-M: 20[redacted] / 491	Y-M: 20[redacted] / 491
CARVEDILOL	12.5 mg	QD	Y-M: 20[redacted] / 492	NOT REPORTED
PHENYTOIN	200 mg	BID	Y-M: 20[redacted] / 493	NOT REPORTED
POTASSIUM	20 mEq	BID	Y-M: 20[redacted] / 493	NOT REPORTED
PRAZOSIN	5 mg	QD	Y-M: 20[redacted] / 493	NOT REPORTED
LEVETIRACETAM	1500 mg	BID	Y-M: 20[redacted] / 493	Y-M: 20[redacted] / 841
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / 495	NOT REPORTED
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 500	NOT REPORTED
ESCITALOPRAM	10 mg	QD	Y-M: 20[redacted] / 507	NOT REPORTED
FISH OIL	2400 mg	QD	Y-M: 20[redacted] / 507	NOT REPORTED
SUCRALFATE	1 g	QID	Y-M: 20[redacted] / 507	NOT REPORTED
PRAZOSIN	2 mg	BID	Y-M: 20[redacted] / 514	NOT REPORTED
PREDNISOLONE	1 %	QD	Y-M: 20[redacted] / 519	NOT REPORTED
SUPREP BOWEL PREP	354 mL	OTHER: ONCE	Y-M: 20[redacted] / 548	Y-M: 20[redacted] / 548
VICODIN	5-325 mg	PRN	Y-M: 20[redacted] / 549	NOT REPORTED
LIDOCAINE	4 %	OTHER: ONCE	Y-M: 20[redacted] / 549	Y-M: 20[redacted] / 549
PROPOFOL	230 mg	OTHER: ONCE	Y-M: 20[redacted] / 549	Y-M: 20[redacted] / 549
VICODIN	5-325 mg	OTHER: ONCE	Y-M: 20[redacted] / 549	Y-M: 20[redacted] / 549
TRAZODONE	50 mg	QD	Y-M: 20[redacted] / 617	NOT REPORTED
LEVETIRACETAM	1500 mg	BID	Y-M: 20[redacted] / 843	NOT REPORTED
LORAZEPAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / 843	Y-M: 20[redacted] / 843
LEVETIRACETAM	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 843	Y-M: 20[redacted] / 844
DIPHENHYDRAMINE	25 mg	QD	Y-M: 20[redacted] / 844	NOT REPORTED
POTASSIUM	40 mEq	OTHER: ONCE	Y-M: 20[redacted] / 844	Y-M: 20[redacted] / 844

OTHER VIRAL VACCINES	0.3 mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 1131	Y-M: 20[redacted]-[redacted] / 1131

Event #1: Serious Adverse Event

Event Description	SEIZURE DISORDER
Preferred Term	痙攣発作
AE Onset Date / Rx Day	[redacted]20[redacted] / 482
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 482): Glucose: 9.7 [4.1 - 5.9] MMOL/L; NPTST333-MAGNESIUM: 2.8 [1.6 - 2.3] MG/DL; Potassium: 2.7 [3.6 - 4.9] MMOL/L; Prothrombin Time: 19 [12 - 15] SEC; [redacted]20[redacted] (Rx Day 485): Leukocytes: 16.1 [3.5 - 10.5] 10^9/L; [redacted]20[redacted] (Rx Day 489): Hemoglobin: 72 [135 - 175] G/L; [redacted]20[redacted] (Rx Day 491): Alanine Aminotransferase: 82 [10 - 46] U/L; Aspartate Aminotransferase: 64 [16 - 37] U/L; NPTST153-CPK: 416 [38 - 174] U/L; [redacted]20[redacted] (Rx Day 493): Alanine Aminotransferase: 102 [10 - 46] U/L; Aspartate Aminotransferase: 93 [16 - 37] U/L; NPTST153-CPK: 242 [38 - 174] U/L

Microbiology

[redacted]20[redacted] (Rx Day 482): BLOOD BLOOD CULTURES: Negative; URINE URINE CULTURE: Positive-LEUKOESTERASE: 2+ PROTEIN: TRACE KETONES: 1+ HEMOGLOBIN: TRACE WBC: 11-20 <10,000 CFU/ML; [redacted]20[redacted] (Rx Day 483): CEREBROSPINAL FLUID MENINGITIS ENCEPHALITIS PANEL P: Negative; CEREBROSPINAL FLUID SPINAL FLUID CULTURE: Negative-NO GROWTH; [redacted]20[redacted] (Rx Day 486): OTHER NASAL SWAB RESPIRATORY PANEL: Negative; [redacted]20[redacted] (Rx Day 491): BLOOD FUNGAL CULTURE: Negative-NO GROWTH AFTER 42 DAYS INCUBATION

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 482): CT ABDOMEN PELVIS:1. MILD DISTAL COLONIC DIVERTICULOSIS WITHOUT ACUTE DIVERTICULITIS, BOWEL OBSTRUCTION, OR ASCITES. 2. MILD TO MODERATE PROSTATE ENLARGEMENT WITH INDENTATION ON THE BLADDER BASE. 3. CHOLELITHIASI; CT OF HEAD:1. NO ACUTE INTRACRANIAL PROCESS IS IDENTIFIED. 2. AGE-RELATED VOLUME LOSS AND NON-SPECIFIC WHITE MATTER HYPOATTENUATION, LIKELY SEQUELA OF CHRONIC MICROVASCULAR ISCHEMIC CHANGE.; MRI OF BRAIN:IMPRESSION: 1. CHRONIC WHITE MATTER ISCHEMIC CHANGES WITHOUT EVIDENCE OF AN ACUTE FINDING.; [redacted]20[redacted] (Rx Day 483): EEG:THIS EEG WAS ABNORMAL DUE TO THE FREQUENT INTERMITTENTLY GENERALIZED SPIKE FOLLOWED UP WITH SLOWED BRAIN WAVE, MORE ON THE RIGHT HEMISPHERE, AND ALSO DEVELOPMENT TO GENERALIZED SPIKE WAVE SUGGESTING T; LUMBAR PUNCTURE:NOT CONSISTENT WITH BACTERIAL MENINGITIS; [redacted]20[redacted] (Rx Day 484): EEG:1. THIS EEG IS ABNORMAL. THE FREQUENTLY GENERALIZED INTERMITTENT SHARP AND FOLLOW UP WITH SLOWED BRAIN WAVE SUGGESTS THERE WAS GENERALIZED EPILEPTOGENIC ABNORMALITY. COMPARED TO EEG STUDY YESTERDAY TH; [redacted]20[redacted] (Rx Day 487): EEG:THIS EEG IS MILDLY ABNORMAL DUE TO SLIGHTLY SLOW BACKGROUND ACTIVITY AND ALSO INTERMITTENTLY SLOWED BRAIN WAVE SUGGESTING THAT THERE IS BILATERAL CEREBRAL DYSFUNCTION. NO SIGNIFICANT EPILEPTIFORM DISC

AE Stopped Rx Day	649 (128 DAYS AFTER LAST TREATMENT)
Duration of AE	168 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SEIZURE MEDICATION WAS STOPPED. DR. BAUM STATES "SEIZURE DISORDER NOT RELATED TO IP. WAS SEEN BY NEURO WHO DIAGNOSED SEIZURE DISORDER, PRESUMABLY IDIOPATHIC AS HE WAS STARTED ON 2 ANTI-EPILEPTIC MEDS.

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

Event #2: Event of Interest - Adjudicated MACE Event, Event of Interest - Adjudicated Extended MACE Event

Event Description	STRESS INDUCED CARIOMYOPATHY
Preferred Term	ストレス心筋症
AE Onset Date / Rx Day	[redacted]20[redacted] / 483
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	488
Duration of AE	6 DAYS
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #3: Event of Interest - Adjudicated MACE Event, Event of Interest - Adjudicated Extended MACE Event

Event Description	CORONARY ARTERY DISEASE-MODERATE
Preferred Term	冠動脈疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 487
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated:[redacted]20[redacted]:09:28
Program Source Code:[redacted]

Investigator No.:[redacted]

Subject Number:[redacted]

Protocol Number: M16-000

米国の治験責任医師からの報告。本被験者は 7[redacted] 歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，発作性疾患の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元紙巻タバコ喫煙者（1 日 1/2 箱を 7 年間），高血圧，片頭痛，クローン病，貧血，心房粗動，心雑音，心房細動及び低カリウム血症であった。

投与 482 日後，被験者は発作性疾患を発現した。投与 649 日後，発作性疾患は消失した。

本事象発現前，被験者は錯乱（非重篤）を発現した。錯乱は 4 日間続き，次第に悪化していた。

投与 482 日後，救急車が要請され，被験者は救急搬送中に痙攣発作を発現した。同日，被験者は入院した。被験者に痙攣発作，脳卒中及び糖尿病の既往歴はなかった。救急治療室での診察中，被験者は全身性強直性間代性発作を突然発症し，発作は約 15 秒間続いた。その後，いびき様呼吸を伴う発作後状態が続き，悪心及び嘔吐もあった。痙攣発作後，Ativan 2 mg が静脈内投与され，Keppra が静脈内投与された。その後，被験者の酸素飽和度は 80%台に低下した。酸素吸入が開始されたが，80%台のままであったため，BiPAP が開始された。INR の補正後，神経科医による診察及び腰椎穿刺が指示された。被験者に当初発熱があったため，髄膜炎を念頭に経験的抗生物質治療が開始された。頭部 CT 検査の結果，異常は認められなかった。頭部 MRI 検査で慢性変化は認められたが，急性の変化の形跡は認められなかった。投与 483 日後，腰椎穿刺が実施され，細菌性髄膜炎と一致していなかった。培養検査及び PCR による髄膜炎パネル検査は陰性であった。EEG で，間欠的な全般性棘波に徐波，全般性棘波と続く異常脳波が右半球優位に頻回に認められ，全般性てんかん様放電が示唆された。Keppra が増量され，Dilantin の投与が開始された。再度の EEG でわずかな改善が認められたが，全般性てんかん様放電が認められた。Dilantin レベルは 12 であった。Keppra 及び Dilantin が増量された。投与 487 日後，再度の EEG で改善が認められた。退院に際し，被験者の神経学的状態は安定しており，ベースラインの状態であった。また，退院時，被験者の意識ははっきりしており，見当識も保たれ，徴候は認められなかった。投与 493 日後，被験者は退院し，Keppra 及び Dilantin の経口投与は継続となった。

被験者は，非 ST 上昇型心筋梗塞（NSTEMI），低カリウム血症の悪化，低酸素症を伴う急性呼吸不全，全身性炎症反応症候群，敗血症，低マグネシウム血症及び膿尿（いずれも非重篤）を発現し，すべて消失した。投与 483 日後，被験者はストレス誘発性心筋症（非重篤）及び正球性貧血と診断された。投与 487 日後，被験者は冠動脈疾患（非重篤）と診断された。

投与された薬剤は，フィトナジオン，新鮮凍結血漿，Cerebyx，Ativan，メラトニン，Phenergan，オムニパーク，硫酸マグネシウム，アセトアミノフェン，リドカイン，Dilantin，Keppra，塩化カリウム及び Zofran であった。

Causality for RISANKIZUMAB (Blinded)

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1) Seizure (10039906) (Seizure (10039906)) [v.23.0] [10039906]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of SEIZURE DISORDER

- Investigator: "Seizure disorder not related to IP. Was seen by Neurologist who diagnosed seizure disorder, presumably idiopathic as he was started on 2 anti-eliptic meds."

- AbbVie: Event is more likely idiopathic as reported by subject matter expert (neurologist). Additionally, the dose of alprazolam was decreased 2 days prior to the event.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALT: 82 No unit

[redacted] 20[redacted] ALT: 102 No unit

[redacted] 20[redacted] AST: 64 No unit

[redacted] 20[redacted] AST: 93 No unit

[redacted] 20[redacted] BLOOD CULTURE: negative

[redacted] **20[redacted] BRAIN MRI:** Chronic white matter ischemic changes without evidence of an acute finding.

[redacted] 20[redacted] C DIFF: Negative

[redacted] 20[redacted] CPK: 416 No unit

[redacted] 20[redacted] CPK: 242 No unit

[redacted] **20[redacted] CRP:** 10.7 mg/dL (normal 0 to 0.9)

[redacted] **20[redacted] CSF CULTURE:** negative: rare white blood cells/LPF; red blood cells observed; no organisms seen

[redacted] 20[redacted] CSF FLUID APPEARANCE: Clear

[redacted] 20[redacted] CSF FLUID COLOR: Colorless

[redacted] **20[redacted] CSF FLUID GLUCOSE:** 65 mg/dL (normal 40 to 70)

[redacted] 20[redacted] CSF FLUID LACTATE DEHYDROGENASE: 34 U/L

[redacted] 20[redacted] CSF FLUID MONOCYTES: 8 %

[redacted] 20[redacted] CSF FLUID POLYS: 92 %

[redacted] **20[redacted] CSF FLUID PROTEIN:** 44 mg/dL (normal 15 to 45)

[redacted] 20[redacted] CSF FLUID RBC: 1160 /CUMM

[redacted] **20[redacted] CSF FLUID WBC:** 4 /CUMM (normal 0 to 5)

[redacted] 20[redacted] CSF VDRL: Negative

[redacted] 20[redacted] CSF WEST NILE AB: Negative

[redacted] **20[redacted] CT ABDOMEN PELVIS:** 1. MILD DISTAL COLONIC DIVERTICULOSIS WITHOUT ACUTE DIVERTICULITIS, BOWEL OBSTRUCTION, OR ASCITES. 2. MILD TO MODERATE PROSTATE ENLARGEMENT WITH INDENTATION ON THE BLADDER BASE. 3. CHOLELITHIASIS WITHOUT ACUTE CHOLECYSTITIS. 4. MILD CARDIOMEGALY WITH MODERATE AORTIC VALVULAR CALCIFICATION AND MULTI VESSEL CORONARY ARTERY CALCIFICATIONS. 5. MILD HEPATOMEGALY. 6. TRACE RIGHT PLEURAL EFFUSION.

[redacted] **20[redacted] CT HEAD:** 1. NO ACUTE INTRACRANIAL PROCESS IS IDENTIFIED. 2. AGE-RELATED VOLUME LOSS AND NON-SPECIFIC WHITE MATTER HYPOATTENUATION, LIKELY SEQUELA OF CHRONIC MICROVASCULAR ISCHEMIC CHANGE.

[redacted] **20[redacted] CXR:** No active cardiopulmonary disease.

[redacted] 20[redacted] DILANTIN LEVEL: 12 No unit

[redacted] **20[redacted] EEG:** This EEG was abnormal due to the frequent intermittently generalized spike followed up with slowed brain wave, more on the right hemisphere, and also development to generalized spike wave suggesting that there is generalized epileptiform discharge.

[redacted] **20[redacted] EEG:** 1. This EEG is abnormal. The frequently generalized intermittent sharp and follow up with slowed brain wave suggests there was generalized epileptogenic abnormality. Compared to EEG study yesterday there was not a major change. 2. The slow background activity also suggests that there is bilateral cerebral dysfunction.

[redacted] **20[redacted] EEG:** This EEG is mildly abnormal due to slightly slow background activity and also intermittently slowed brain wave suggesting that there is bilateral cerebral dysfunction. No significant epileptiform discharges occurred. Compared to EEG a few days ago it has had significant improvement.

[redacted] **20[redacted] EGD:** Non-bleeding duodenal ulcers.

[redacted] 20[redacted] FUNGUS CULTURE: negative

[redacted] **20[redacted] GLUCOSE:** 174 mg/dL (normal 74 to 106)

[redacted] 20[redacted] HEART RATE: 107 BPM

[redacted] **20[redacted] HEMOGLOBIN:** 7.2 G/DL (normal 13.5 to 17.5)

[redacted] **20[redacted] HEMOGLOBIN:** 7.6 G/DL (normal 13.5 to 17.5)

[redacted] **20[redacted] LUMBAR PUNCTURE:** not consistent with bacterial meningitis

[redacted] **20[redacted] MAGNESIUM:** 2.8 mg/dL (normal 1.6 to 2.3)

[redacted] 20[redacted] MENINGITIS ENCEPHALITIS PANEL: negative

[redacted] **20[redacted] POTASSIUM:** 2.7 MMOL/L (normal 3.6 to 4.9)

[redacted] **20[redacted] PROCALCITONIN:** 0.05 ng/mL (normal 0 to 0.09)

[redacted] **20[redacted] PT:** 19.4 SEC (normal 11.8 to 14.8)

[redacted] 20[redacted] RESPIRATORY PCR PANEL: Negative

[redacted] 20[redacted] RESPIRATORY RATE: 22 MIN

[redacted] 20[redacted] SPO2: 98 %

[redacted] 20[redacted] TEMPERATURE: 98.0 degrees F

[redacted] **20[redacted] TTE:** The quality of the study was technically difficult, poor despite the use of contrast, and endocardial definition remains poor. The left ventricular chamber size is normal. The left ventricular systolic function is severely decreased. The visually estimated ejection fraction is between 25-30%. The LV function suggested apical ballooning. There is mild to moderate aortic stenosis. There is mild aortic valve regurgitation. There is mild mitral valve regurgitation. There is mild tricuspid valve regurgitation. The right ventricular systolic pressure is 35 mmHg.

[redacted] **20[redacted] URINE CULTURE:** Positive; leukoesterase: 2+; protein: trace; ketones: 1+; hemoglobin: trace; wbc: 11-20; <10,000 CFU/ML

[redacted] 20[redacted] URINE CULTURE: contaminated

[redacted] 20[redacted] URINE CULTURE: <10,000 CFU/mL

[redacted] **20[redacted] US RENAL COMPLETE W/AO AND NODES:** 1. Enlarged prostate impresses upon bladder base. 2. Simple renal cysts. 3. No hydronephrosis or perinephric fluid collection.

[redacted] **20[redacted] WBC:** 16.1 X10**9/L (normal 3.5 to 10.5)

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
播種性ヒストプラスマ症	X			X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	2[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: ANEMIA OF CHRONIC DISEASE	20[redacted]
OTHER: ALLERGY TO MORPHINE	20
OTHER: ALLERGY TO PENICILLIN	20
OTHER: HYPOKALEMIA	20
OTHER: HYPONATREMIA	20
OTHER: INTERMITTENT DEHYDRATION	20
CROHN'S DISEASE	20
OTHER: JOINT PAIN	20
OTHER: PERIPHERAL ARTHROPATHY	20
OTHER: ACUTE RENAL FAILURE	20
OTHER: ALLERGY TO CODEINE	20
HYPERTENSION	20
OTHER: CHRONIC BACK PAIN	20
OTHER: DYSPNEA ON EXERTION	20

Prior Procedures	Procedure Year
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 33	[redacted] / 33	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 33	[redacted] / 33	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 61	[redacted] / 61	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 61	[redacted] / 61	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 92	[redacted] / 92	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 151	[redacted] / 151	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 209	[redacted] / 209	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 263	[redacted] / 263	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted] / 278	[redacted] / 278	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 321	[redacted] / 321	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 372	[redacted] / 372	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 431	[redacted] / 431	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
VEDOLIZUMAB	300 mg	OTHER: DOSE AT WK 0, WK 2, AND WK 6	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: DOSE AT WK 0, WK 2, WK 6	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -63

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
GOLYTELY	236 g	OTHER: ONCE	Y-M: 20[redacted] / 459	Y-M: 20[redacted] / 459

PROPOFOL	900 mg	OTHER: ONCE	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 460
ITRACONAZOLE	200 mg	TID	Y-M: 20[redacted] / 475	Y-M: 20[redacted] / 641
MESALAZINE	800 mg	TID	Y-M: 20[redacted] / 483	ONGOING
ITRACONAZOLE	200 mg	BID	Y-M: 20[redacted] / 641	Y-M: 20[redacted] / 1007

Event #1: Serious Adverse Event, Event of Interest - Serious Infections, Event of Interest - Opportunistic Infections (includes fungal infections)

Event Description	DISSEMINATED HISTOPLASMOSIS
Preferred Term	播種性ヒストプラスマ症
AE Onset Date / Rx Day	[redacted]20[redacted] / 460 (29 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 475): C Reactive Protein: 1.1 [NOT REPORTED - 0.9] mg/dL; Hemoglobin: 83 [135 - 175] G/L; Monocytes/Leukocytes: 9.8 [2 - 9] %; NPTST233-FUNGITELL: 56 [NOT REPORTED - 80] PG/ML; NPTST287-HISTOPLASMA GALACTOMANNAN ANTIG: <0.5 [NOT REPORTED - 0.5] ng/mL; NPTST287-HISTOPLASMA GALACTOMANNAN ANTIG: <0.5 [NOT REPORTED - 0.5] ng/mL; NPTST481-SED RATE: 31 [NOT REPORTED - 15] mm/h; NPTST512-T-SPOT TB TEST: NEGATIVE [NOT REPORTED - NOT REPORTED] RESULTS ARE EITHER NEGATIVE OR

Microbiology

[redacted]20[redacted] (Rx Day 460): OTHER COLONIC MUCOSA GRAM STAIN, PAS AND SILVER METH: Positive-FINAL DIAG: COLONIC MUCOSA (COLON POLYPS, MULTIPLE): 1. INFLAMMATORY PSEUDOPOLYPS, WITH SOME POLYPS SHOWING SURFACE EROSION AND MARKED INVOLVEMENT BY FUNGAL SPORES SUGGESTIVE OF HISTOPLASMA; [redacted]20[redacted] (Rx Day 475): BLOOD FUNGAL CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 460): COLONOSCOPY:ACTIVE INFLAMMATION WITHIN THE RECTUM WITH CONGESTED, ERYTHEMATOUS AND ERODED MUCOSA IN THE RECTUM. OTHER THAN PSEUDOPOLYPS THERE WAS MILD INFLAMMATION WITH

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	NO
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:09:28
Program Source Code: [redacted]

Investigator No.: [redacted]