The patient's past medications include:

PREDNISONE for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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

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

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

Dechallenge: Not Applicable

2) Intestinal stricture (10022701) (Intestinal stenosis (10022699)) [v.22.1] [10022701]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

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

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

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

Dechallenge: Not Applicable

2) Intestinal stricture (10022701) (Intestinal stenosis (10022699)) [v.22.1] [10022701]

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 CROHN'S STRICTURE

- Investigator: Crohn's disease.

- AbbVie: Risk factor includes pre-existing Crohn's disease.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of CROHN'S STRICTURE

- Investigator: CROHN'S DISEASE

- AbbVie: Risk factor includes pre-existing Crohn's disease.

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes Zoster: Location, number of dermatomes, and dissemination not reported.

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
足関節部骨折	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	4[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: ARTHRALGIA - JOINTS, BODY, BACK, LEGS, BUTT	19[redacted]
CROHN'S DISEASE	19[redacted]
OTHER: DIARRHEA	19[redacted]
EYE DISEASE/DISORDER: ORBITAL MYOSITIS	20[redacted]
OTHER: BROKEN RIBS - T3	20[redacted]
OTHER: PERIANAL FISTULA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	19[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	19[redacted]
CROHN'S DISEASE SURGICAL HISTORY: REANASTOMOSIS	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	24 CIGARETTE	35	
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)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 62	[redacted]20[redacted] / 62	1

M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
M15991 /RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 114	[redacted]20[redacted] / 114	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 135	[redacted]20[redacted] / 135	1
M15991 /RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 135	[redacted]20[redacted] / 135	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 162	[redacted]20[redacted] / 162	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 212	[redacted]20[redacted] / 212	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 273	[redacted]20[redacted] / 273	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 330	[redacted]20[redacted] / 330	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 345	[redacted]20[redacted] / 345	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 386	[redacted]20[redacted] / 386	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 448	[redacted]20[redacted] / 448	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 498	[redacted]20[redacted] / 498	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ADALIMUMAB	160 mg	OTHER: ONCE, WEEK 0	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: ONCE, WEEK 2	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
PARACETAMOL	1500-2000 mg	TID	Y-M: 20[redacted] / 1
BUPROPION	150MG X 3DAYS THE 300MG DAILY mg	QD	Y-M: 20[redacted] / 160

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
MORPHINE	1 OTHER: DOSE	PRN	Y-M: 20[redacted] / 349	Y-M: 20[redacted] / 350

ULTRACET	2 OTHER: PILLS	PRN	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 353
COLESTIPOL	2-4 g	PRN	Y-M: 20[redacted] / 386	ONGOING

Event #1: Serious Adverse Event

Event Description	LEFT ANKLE FRACTURE
Preferred Term	足関節部骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 347
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx Day 379): LEFT ANKLE FRACTURE REPAIR:FRACTURE WAS REPAIRED	
AE Stopped Rx Day	399
Duration of AE	53 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	FARM EQUIPMENT/ WORK INJURY
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]

Subject Number: [redacted]

Protocol Number: M16-000

カナダ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及びリサンキズマブが投与され，左足関節部骨折の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病（回腸結腸，狭窄型），現喫煙者（1 日 24 本を 35 年間）及び現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はレスキュー治療としてリサンキズマブの非盲検投与を受けた。

投与 347 日後，被験者は左足関節部骨折を発現した。投与 399 日後，左足関節部骨折は消失した。

投与 347 日後，被験者は仕事関連の外傷で足関節部を骨折した。疼痛のため，被験者は救急治療室を受診した。左足関節部 X 線検査が行われ，骨折が確認された。投与 349 日後，被験者は左足関節部骨折の外科的修復術のため日帰り入院した。投与 350 日後，被験者は退院した。

投与された薬剤は，モルヒネ及び Tramacet であった。

The patient's past medications include:

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])

Causality for RISANKIZUMAB (Blinded)

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1) Ankle fracture (10002544) (Ankle fracture (10002544)) [v.23.0] [10002544]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

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1) Ankle fracture (10002544) (Ankle fracture (10002544)) [v.23.0] [10002544]

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 LEFT ANKLE FRACTURE

- Investigator: Farm equipment/ work injury

- AbbVie: Event more likely related to trauma from farm equipment/work injury, as reported by the investigator.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of LEFT ANKLE FRACTURE

- Investigator: Farm equipment/ work injury

- AbbVie: Event more likely related to trauma from farm equipment/work injury, as reported by the investigator.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ANKLE X-RAY: Fracture

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
心不全	X			
クローン病	X			
帯状疱疹				X
肺腺癌	X	X		X
骨転移		X		X

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	6[redacted]	MALE	WHITE

Medical History	Onset Year
EYE DISEASE/DISORDER: AWAITING CATARACT SURGERY	NOT REPORTED
OTHER: MILD DEHYDRATION	NOT REPORTED
OTHER: EX SMOKER- STOPPED IN 19[redacted].	19[redacted]
OTHER: EX-SMOKER	19[redacted]
PNEUMONIA	20[redacted]
OTHER: POLYNEUROPATHY DISORDER	20[redacted]
OTHER: SENSORY ATAXIA	20[redacted]
OTHER: SENSORY ATAXIA - ATTENDS NEUROLOGY	20[redacted]
PERIPHERAL NERVE DISORDER: POLYNEUROPATHY DISORDER- SAME IS HEREDITARY - LOWER LIMB SENSORY NEUROPATHY	20[redacted]
OTHER: IGM MONOCLONAL GAMMOPATHY	20[redacted]
OTHER: ABDOMINAL CRAMPS SECONDARY TO CROHNS DISEASE	20[redacted]
HYPERTENSION	20[redacted]
OTHER: LEFT BUNDLE BRANCH BLOCK	20[redacted]
ANGINA	20[redacted]
CORONARY ARTERY DISEASE: HIGH CHOLESTEROL	20[redacted]
DEPRESSION: MILD DEPRESSION- ON LEXAPRO FOR SAME	20[redacted]
OTHER: ACID REFLUX	20[redacted]
OTHER: CORONARY ANGIOGRAM SHOWED PROXIMAL 50-60% LAD STENOSIS	20[redacted]
OTHER: DILATED CARDIOMYOPATHY	20[redacted]
OTHER: HYPERLIPEMIA. ON LIPITOR	20[redacted]
OTHER: HYPERLIPIDEMIA	20[redacted]
CORONARY ARTERY DISEASE: 50-60% STENOSIS TO LAD	20[redacted]
OTHER: MITRAL REGURGITATION	20[redacted]
OTHER: MITRAL REGURGITATION. ATTENDS CARDIOLOGY REGULARLY	20[redacted]
OTHER: HIATUS HERNIA	20[redacted]
OTHER: HIATUS HERNIA-NIL TREATMENT	20[redacted]

ANEMIA: IRON DEFICIENCY ANAEMIA	20[redacted]
OTHER: B12 DEFICIENCY	20[redacted]
CROHN'S DISEASE	20[redacted]
EYE DISEASE/DISORDER: CATARACT	20[redacted]
INFLAMMATORY BOWEL DISEASE: HIGH STOOL FREQUENCY	20[redacted]
OTHER: ABDOMINAL CRAMPING PAIN SECONDARY TO CROHN'S DISEASE	20[redacted]
OTHER: LOW MAGNESIUM LEVEL	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	19[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	35 CIGARETTE	24	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 87	[redacted]20[redacted] / 87	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 141	[redacted]20[redacted] / 141	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 205	[redacted]20[redacted] / 205	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 260	[redacted]20[redacted] / 260	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: 19[redacted]
ACETYLSALICYLIC ACID	75 mg	QD	Y-M: 20[redacted]
ATORVASTATIN	80 mg	QD	Y-M: 20[redacted]
BISOPROLOL	6.25 mg	QD	Y-M: 20[redacted]
ESCITALOPRAM	5 mg	QD	Y-M: 20[redacted]
GLYCERYL TRINITRATE	400 OTHER: MCG	PRN	Y-M: 20[redacted]
ISOSORBIDE MONONITRATE	50 mg	QD	Y-M: 20[redacted]
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted]
PERINDOPRIL	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
BISOPROLOL	6.25 mg	QD	Y-M: 20[redacted]	ONGOING
PERINDOPRIL	5 mg	QD	Y-M: 20[redacted]	ONGOING
CLOPIDOGREL	300 mg	OTHER: STAT	Y-M: 20[redacted] / 99	Y-M: 20[redacted] / 99
CLOPIDOGREL	300 mg	QD	Y-M: 20[redacted] / 99	Y-M: 20[redacted] / 99
BISOPROLOL	1.25 mg	OTHER: STAT	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 100
HEPARIN	2,000 IU	OTHER: STAT	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 100
MIDAZOLAM	2 mg	OTHER: STAT	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 100
PERINDOPRIL	2.5 mg	OTHER: STAT	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 100
VERAPAMIL	2.5 mg	OTHER: STAT	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 100
FLUTICASONE	50 OTHER: MCG	PRN	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 121
BISOPROLOL	7.5 mg	QD	Y-M: 20[redacted] / 101	ONGOING
PERINDOPRIL	7.5 mg	QD	Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 234
INFLUENZA VACCINE	60 OTHER: MCG	OTHER: STAT	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 109
FAMCICLOVIR	250 mg	BID	Y-M: 20[redacted] / 152	Y-M: 20[redacted] / 159
RIVAROXABAN	15 mg	BID	Y-M: 20[redacted] / 205	Y-M: 20[redacted] / 226
OLMESARTAN	10 mg	QD	Y-M: 20[redacted] / 224	ONGOING

RIVAROXABAN	20 mg	QD	Y-M: 20[redacted] / 226	ONGOING
EPLERENONE	25 mg	QD	Y-M: 20[redacted] / 232	Y-M: 20[redacted] / 334
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / 234	ONGOING
FENTANYL	75 OTHER: MCG	OTHER: STAT	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 298
LIDOCAINE	1 /10 %	OTHER: STAT	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 298
MIDAZOLAM	4 mg	OTHER: STAT	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 298
EPLERENONE	50 mg	QD	Y-M: 20[redacted] / 335	ONGOING
ERLOTINIB	150 mg	QD	Y-M: 20[redacted] / 339	ONGOING
CALCIUM CARBONATE	500 mg	QD	Y-M: 20[redacted] / 344	ONGOING
CYANOCOBALAMIN	1000 mg	PRN	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 344
DENOSUMAB	120 mg	OTHER: MONTHLY	Y-M: 20[redacted] / 347	ONGOING
SODIUM CHLORIDE	1000 mL	OTHER: STAT	Y-M: 20[redacted] / 351	Y-M: 20[redacted] / 351
HYDROCORTISONE	100 mg	TID	Y-M: 20[redacted] / 351	Y-M: 20[redacted] / 354
SODIUM CHLORIDE	1000 mL	OTHER: STAT	Y-M: 20[redacted] / 352	Y-M: 20[redacted] / 352
PHOSPHORIC ACID	250 mL	OTHER: STAT	Y-M: 20[redacted] / 353	Y-M: 20[redacted] / 353
MAGNESIUM	250 mL	OTHER: STAT	Y-M: 20[redacted] / 354	Y-M: 20[redacted] / 354

Event #1: Serious Adverse Event

Event Description CARDIAC FAILURE STAGE II

Preferred Term 心不全

AE Onset Date / Rx Day [redacted]20[redacted] / 98

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 99): Hemoglobin: 122 [130 - 170] G/L; NPTST531-TROPONIN: 10 [3 - 14] NG/ML; 20[redacted] (Rx Day 100): NPTST531-TROPONIN: 9 [3 - 14] NG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 99): ECHO:EJECTION FRACTURE 41%.; [redacted]20[redacted] (Rx Day 100): CORONARY ANGIOGRAM:MILD NON OBSTRUCTIVE CAD; ECG:SINUS RHYTHM WITH LBBB AT 72 BPM

AE Stopped Rx Day ONGOING

Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PATIENT HAS CARDIAC BACKGROUND. AWAITING ANGIO FOR FURTHER INFORMATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Herpes Zoster

Event Description	SHINGLES - ON CHEST X 1 DERMATOME
Preferred Term	帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 151
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Rx Day	160
Duration of AE	10 DAYS
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	ADENOCARCINOMA OF THE LEFT LUNG
Preferred Term	肺腺癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 290 (30 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 290): Albumin: 33 [35 - 50] G/L; Hemoglobin: 119 [130 - 170] G/L; NPTST558-VITAMIN D: 22 [30 - 125] NMOL/L; [redacted]20[redacted] (Rx Day 324): Alkaline Phosphatase: 152 [30 - 130] U/L; Hematocrit: 0 [0 - 0.01] FRACTION OF 1; Leukocytes: 12.8 [3.5 - 11] 10^9/L; NPTST374-NEUTROPHILS: 10.5 [2 - 8] 10^9/L; NPTST457-RED CELL COUNT: 4.13 [4.5 - 5.5] 10^12/L

Microbiology

[redacted]20[redacted] (Rx Day 298): OTHER BRUSHINGS FROM LINGULA, WASHINGS FROM LINGULA AND ENDOBROCHIAL BIOPSY FROM LINGULA BRONCHIAL WASHINGS AND BRUSHING: -LARGE MALIGNANT CELLS IN BOTH SAMPLES. SINGULAR AND CLUSTERS, CONSISTENT WITH NON SMALL CELL LUNG CANCER (NSCLC); OTHER LUNG BIOPSY HISTOPATHOLOGY BIOPSY:

Positive-PULMONARY ADENOCARCINOMA; OTHER MICROBIOLOGY MOLECULAR TESTING OF BIOPSY: Positive-EGFR ON EXON 21 L858R SENSITIZING WAS IDENTIFIED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 290): CHEST X RAY:CHEST IMAGING DEMONSTRATED LEFT MID ZONE INFILTRATE AND "ARTEFACT" TO RIGHT PROXIMAL HUMERUS; CT THORAX:IS SUSPICIOUS FOR A LEFT HILAR CARCINOMA WITH INVASION INTO THE MEDIASTINUM, LIKELY SQUAMOUS OR A MUCINOUS ADENOCARCINOMA WITH EXTENSIVE LYMPHANGITIS THROUGHOUT THE LEFT LUNG AND CONTRALATERAL SMALL L; [redacted]20[redacted] (Rx Day 298): BRONCHOSCOPY:THERE WAS AN OBSTRUCTING LESION IN THE LINGULA AND SOME NARROWING OF THE LEFT UPPER LOBE AND ALSO THE LEFT LOWER LOBE.BIOPSY HAS SINCE SHOWN ADENOCARCINOMA AND FURTHER STAINING HAS BEEN SENT.; [redacted]20[redacted] (Rx Day 312): PET SCAN:THERE IS A 6.9CM HILAR MASS, MEDIASTINAL AND CONTRALATERAL SUPRACLAVICULAR LYMPH ADENOPATHY (N3), POSSIBLE LIVER METASTASES AND MULTIPLE BONE METASTASES INCLUDING IN VERTEBRAE T11,L2 AND L4 AND IN THE; [redacted]20[redacted] (Rx Day 324): X RAY OF HIPS, FEMORA AND PELVIS:THERE IS A 1CM SCLEROTIC FOCUS IN THE RIGHT PROXIMAL FEMUR (INTERTROCHANTERIC AREA). FURTHER 1CM SCLEROTIC FOCUS IN THE PROXIMAL LEFT FEMUR SUB TROCHANTERIC AREA. THESE ARE SUSPICIOUS FOR METASTATIC L

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	FAMILY HISTORY OF CANCER
Discontinued Study Drug Due to the Event	YES
SAE Criteria	LIFE THREATENING

Event #4: AE Leading to Discontinuation of Study Drug, Event of Interest - Malignancies

Event Description	BONY METASTASIS TO BILATERAL HIPS
Preferred Term	骨転移
AE Onset Date / Rx Day	[redacted]20[redacted] / 326 (66 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #5: Serious Adverse Event

Event Description	FLARE OF CROHNS
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 353 (93 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (Rx Day 352): STOOL FAECAL CALPROTECTIN: Positive-270; STOOL MICROBIOLOGY-RECTAL SWAB FOR VR: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 351): ABDOMINAL X-RAY:SCLEROTIC FOCI NOTED IN RIGHT PROXIMAL FEMUR AND LEFT SACRUM IN KEEPING WITH PATIENTS KNOWN METASTASIS; [redacted]20[redacted] (Rx Day 353): ABDOMINAL X-RAY:NO OBSTRUCTION. CROHNS NOTED DUE TO SENTINAL LOOP

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	FLARE OF CROHNS AS STOPPED RISANKISUMAB DUE TO SAE OF LUNG CANCER. COLITIS INDUCED ALSO FROM IMMUNOTHERAPY. DIARRHOEA KNOWN SIDE EFFECT.
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

アイルランド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，ステージ II の心不全の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元喫煙者（1 日 35 本を 24 年間），高血圧，左脚ブロック，アンギナ，拡張型心筋症，コレステロール高値，高脂血症，冠動脈疾患，左冠動脈前下行枝狭窄（50～60%），僧帽弁逆流，クローン病，マグネシウム低値及び飲酒者（1 日 2 杯未満）であった。

投与 98 日後，被験者はステージ II の心不全を発現した。

投与 98 日後，被験者は労作時の胸痛，動悸，及び呼吸困難のため入院した。血液検査，ECG 及びエコー検査が行われた。被験者は血管造影も受け，その結果，軽度の非閉塞性冠動脈疾患が認められた。被験者は急速進行性アンギナ，及び安静狭心症を含むアンギナの非定型症状を呈していた。被験者は心臓病科で厳密にモニタリングされ，移動可能であった。投与 100 日後，被験者は退院した。

投与された薬剤は，ペリンドプリル，クロピドグレル，ミダゾラム，ヘパリン，ベラパミル及びビソプロロールであった。

Causality for RISANKIZUMAB (Blinded)

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1) Cardiac failure (10007554) (Cardiac failure (10007554)) [v.23.1] [10007554]

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 CARDIAC FAILURE STAGE II

- Investigator: Patient has cardiac background, awaiting angio for further information

- AbbVie: Event is more likely related to pre-existing history of dilated cardiomyopathy. Pre-existing hypertension, coronary artery disease, and mitral regurgitation are additional risk factors.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANGIOGRAM:** Mild non obstructive CAD.

[redacted] 20[redacted] CORONARY ANGIOGRAM: Mild non-obstructive CAD

[redacted] 20[redacted] ECG: Normal

[redacted] **20[redacted] ECG:** Sinus Rhythm with LBBB AT 72 bpm

[redacted] 20[redacted] ECHOCARDIOGRAM: ejection fraction 41%

[redacted] **20[redacted] TROPONIN:** 10 NG/DL (normal 3 to 14)

[redacted] **20[redacted] TROPONIN:** 9 NG/DL (normal 3 to 14)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

アイルランド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及びリサンキズマブが投与され，左肺腺癌の事象を発現した。

Event 3 の臨床経過：

関連する病歴は，元喫煙者（1 日 35 本を 24 年間），高血圧，左脚ブロック，呑酸，アンギナ，拡張型心筋症，高脂血症，冠動脈疾患，僧帽弁逆流，クローン病，現飲酒者（1 日 2 杯未満）及び癌の家族歴であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はレスキュー治療としてリサンキズマブの非盲検投与を受けた。

投与 290 日後，被験者は左肺腺癌を発現した。

投与 260 日後，咳嗽が持続しているため，被験者は胸部 X 線検査を受けた。その後，被験者は肺炎と診断され，抗生剤による治療を受けたが，改善しなかった。投与 291 日後，再度行われた胸部 X 線検査の結果，改善は認められなかった。そのため，胸部 CT 検査が行われた。胸部 CT 検査の結果，肺癌の診断が確定した。投与 298 日後，気管支鏡検査が行われた。その結果，肺小舌の閉塞病変，並びに左肺上葉及び左肺下葉のやや狭小化が認められた。生検の結果，腺癌が認められ，さらなる染色検査に送られた。また，投与 312 日後，PET スキャン検査の結果，肺門腫瘤（6.9 cm），縦隔及び反対側の鎖骨上リンパ節症（N3），肝転移の可能性，並びに椎骨 T11，L2，L4，骨盤骨内，左大腿骨近位部及び右大腿骨頚部を含む複数の骨転移が認められた。PET による病期分類は T3N31C であった。

本事象に関連するリスク因子は，被験者が元喫煙者（24 年間）であることであった。

投与された薬剤は，エルロチニブ及びデノスマブであった。

The patient's past medications include:

AMOXICILLIN for PNEUMONIA ([redacted])

AUGMENTIN for PNEUMONIA ([redacted])

DOXYCYCLINE for PNEUMONIA ON CHEST X RAY ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Adenocarcinoma lung (10001160) (Lung adenocarcinoma (10025031)) [v.24.0] [10001160]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

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1) Adenocarcinoma lung (10001160) (Lung adenocarcinoma (10025031)) [v.24.0] [10001160]

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 ADENOCARCINOMA OF THE LEFT LUNG

- Investigator: Family History of Cancer

- AbbVie: 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]). Additionally, weak temporal association with approximately 8.5 months of study drug exposure and subject's significant past smoking history.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of ADENOCARCINOMA OF THE LEFT LUNG

- Investigator: Family History of Cancer

- AbbVie: 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]). Additionally, weak temporal association with approximately 8.5 months of study drug exposure and subject's significant past smoking history.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 33 G/L (normal 35 to 50)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 152 IU/L (normal 30 to 130)

[redacted] **20[redacted] BRONCHOSCOPY:** There was an obstructing lesion in the lingula and some narrowing of the left upper lobe and also the left lower lobe. Biopsy has been since shown adenocarcinoma and further staining has been sent.

[redacted] 20[redacted] CHEST X-RAY: Pneumonia.

[redacted] **20[redacted] CHEST X-RAY:** Progression of consolidation. Chest imaging demonstrated left mid zone infiltrate and "artefact" to right proximal humerus.

[redacted] **20[redacted] CHEST X-RAY:** Post-antibiotic therapy. Showed no improvement.

[redacted] **20[redacted] CT THORAX:** Suspicious for a left hilar carcinoma with invasion into the mediastinum, likely squamous or a mucinous adenocarcinoma with extensive lymphangitis throughout the left lung and contralateral small lung metastases with N3 nodal disease and multiple suspected bony mets. Provisional staging based on imaging alone would be T3 N3 M1C

[redacted] 20[redacted] ENDOBRONCHIAL BIOPSY: Pulmonary Adenocarcinoma

[redacted] **20[redacted] HEMATOCRIT:** 0.351 L/L (normal 0.4 to 0.5)

[redacted] **20[redacted] HEMOGLOBIN:** 11.9 G/DL (normal 13 to 17)

[redacted] **20[redacted] LUNG BIOPSY:** Histopathology biopsy- positive pulmonary adenocarcinoma

[redacted] **20[redacted] MOLECULAR TESTING OF BIOPSY:** Positive-EGFR ON EXON 21 L858R SENSITIZING WAS IDENTIFIED

[redacted] **20[redacted] NEUTROPHILS:** 10.5 X10**9/L (normal 2 to 8)

[redacted] **20[redacted] PET SCAN:** THERE IS A 6.9CM HILAR MASS, MEDIASTINAL AND CONTRALATERAL SUPRACLAVICULAR LYMPH ADENOPATHY (N3), POSSIBLE LIVER METASTASES AND MULTIPLE BONE METASTASES INCLUDING IN VERTEBRAE T11,L2 AND L4 AND IN THE PELVIC BONES, THE PROXIMAL LEFT FEMUR AND RIGHT FEMORAL NECK. THE PET STAGING IS T3N3M1C

[redacted] **20[redacted] RED CELL COUNT:** 4.13 X10**12/L (normal 4.5 to 5.5)

[redacted] **20[redacted] VITAMIN D:** 22 NMOL/L (normal 30 to 125)

[redacted] **20[redacted] WHITE BLOOD CELLS COUNT:** 12.8 X10**9/L (normal 3.5 to 11)

[redacted] **20[redacted] X-RAY OF HIPS, FEMORA AND PELVIS:** THERE IS A 1CM SCLEROTIC FOCUS IN THE RIGHT PROXIMAL FEMUR (INTERTROCHANTERIC AREA). FURTHER 1CM SCLEROTIC FOCUS IN THE PROXIMAL LEFT FEMUR SUB TROCHANTERIC AREA. THESE ARE SUSPICIOUS FOR METASTATIC LESIONS. NO FRACTURES. SMALL SCLEROTIC FOCUS IN THE PROXIMAL RIGHT TIBIA MAY REPRESENT A BONE ISLAND

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

アイルランド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及びリサンキズマブが投与され，クローン病のフレアの事象を発現した。

Event 5 の臨床経過：

関連する病歴は，元喫煙者（1 日 35 本を 24 年間），クローン病に続発した腹部仙痛，呑酸，高脂血症，裂孔ヘルニア，ビタミン B12 欠乏，クローン病（回腸，非狭窄型，非穿通型）及び現飲酒者（1 日 2 杯未満）であった。

20[redacted]年[redacted]月[redacted]日，レスキュー治療としてリサンキズマブの非盲検投与が開始された。

投与 353 日後，被験者はクローン病のフレアを発現した。

投与 351 日後，被験者は，疲労，血液を伴う排便回数増加（10～14 回），及びクローン病のフレア又はタルセバ誘発性大腸炎のため，入院した。診断検査及び画像検査が行われた。

被験者は，静脈内補液，ヒドロコルチゾン，及びウステキヌマブの静脈内投与による治療を受けた。電解質失調後，被験者の血液は改善した。便検体は正常であり，感染は検出されず，

便中カルプロテクチンは 270 であった。ステロイド剤は漸減され，投与 354 日後，被験者は退院した。

投与された薬剤は，プレドニゾロン，prednisone，塩化ナトリウム，生理食塩液＋12 mmol リン酸塩，ヒドロコルチゾン，Magnesium Sona，生理食塩液＋4 g マグネシウム及びウステキヌマブであった。

Causality for RISANKIZUMAB (Blinded)

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1) Crohn's aggravated (10011399) (Crohn's disease (10011401)) [v.23.0] [10011399]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

---

1) Crohn's aggravated (10011399) (Crohn's disease (10011401)) [v.23.0] [10011399]

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 FLARE OF CROHNS

- Investigator: Flare of crohns as stopped risankisumab due to sae of lung cancer. Colitis induced also from immunotherapy. Diarrhoea known side effect.

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

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of FLARE OF CROHNS

- Investigator: Flare of crohns as stopped risankisumab due to sae of lung cancer. Colitis induced also from immunotherapy. Diarrhoea known side effect.

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

Relevant Laboratory & Other Diagnostic Tests

20[redacted] BLOOD UREA: High

[redacted] **20[redacted] CULTURE:** rectal swab for VRE (vancomycin resistant Enterococcus) / CPE (carbapenemase producing enterobacteria) - negative

[redacted] 20[redacted] FECAL CALPROTECTIN: Positive - 270

[redacted] **20[redacted] X-RAY ABDOMEN:** sclerotic foci noted in right proximal femur and left sacrum in keeping with patient's known metastasis

[redacted] **20[redacted] X-RAY ABDOMEN:** no obstruction, Crohn's noted due to sentinel loop

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes Zoster: Located on the chest. One dermatome noted. Dissemination not reported.

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 M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
HEPATITIS: PRIMARY SCLEROSING CHOLANGITIS	20[redacted]
OTHER: PERIPHERAL ARTHRALGIA	20[redacted]
ANEMIA: MODERATE ANEMIA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CAESEREAN	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1

M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85	1
M15991 /RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 115	[redacted]20[redacted] / 115	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 148	[redacted]20[redacted] / 148	1
M15991 /RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 148	[redacted]20[redacted] / 148	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 171	[redacted]20[redacted] / 171	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 260	[redacted]20[redacted] / 260	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 319	[redacted]20[redacted] / 319	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 365	[redacted]20[redacted] / 365	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 457	[redacted]20[redacted] / 457	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 486	[redacted]20[redacted] / 486	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 514	[redacted]20[redacted] / 514	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: 19[redacted]
URSODEOXYCHOLIC ACID	250 mg	BID	Y-M: 20[redacted]
MESALAZINE	800 mg	TID	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
PANCREATIN	420 mg	TID	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 250
SMECTA	3 g	TID	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 250
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 268	Y-M: 20[redacted] / 277
IRON	2 mL	OTHER: N.7(ONCE IN 2 DAYS - IN ODD DAYS)	Y-M: 20[redacted] / 268	Y-M: 20[redacted] / 282

OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 268	Y-M: 20[redacted] / 282
IMIDAZOLYL ETHANAMIDE PENTANDIOIC ACID	90 mg	QD	Y-M: 20[redacted] / 281	Y-M: 20[redacted] / 286

Event #1: Serious Adverse Event

Event Description	EXCEREBRATION OF CD
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 263
Age at AE Onset	3[redacted]
Laboratory Testing	[redacted]20[redacted] (Rx Day 263): Tryptase: 6.6 [2.2 - 13.2] UG/L; [redacted]20[redacted] (Rx Day 268): Hemoglobin: 76 [120 - 150] G/L; [redacted]20[redacted] (Rx Day 271): Hemoglobin: 101 [120 - 150] G/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (Rx Day 270): BLOOD TRANSFUSION (ERYTHROCYTE MASS WITH A REMOVED LEUKOCYTE AND PLATELET LAYER 506 ML):IMPROVEMENT OF WELL-BEING; [redacted]20[redacted] (Rx Day 275): ECG:BRADICARDIA; ULTRASOUND ABDOMINAL:NORMAL
AE Stopped Rx Day	282
Duration of AE	20 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	COMPLICATED COURSE OF CHRON'S DISEASE
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

ロシア連邦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 1 の臨床経過：

関連する病歴は，クローン病，中等度の貧血，非喫煙者及び禁酒であった。

投与 263 日後，被験者はクローン病増悪を発現した。投与 282 日後，クローン病増悪は消失した。

投与 268 日後，皮下投与の 3 日後，被験者は，重度の腸管外症状（貧血及び原発性硬化性胆管炎）を伴うクローン病増悪を発現した。被験者は，血管炎，関節炎，下痢，高体温及び直腸出血を発現した。被験者にアナフィラキシー検査を行うことが決定された。投与 270 日後，輸血が行われた。アナフィラキシーは除外された。投与 282 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，オメプラゾール，プレドニゾロン，赤血球，フェインジェクト及びファモチジンであった。

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 CD

- Investigator: Not reported.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL ULTRASOUND: Normal

20[redacted] ABDOMINAL ULTRASOUND: Not reported.

[redacted] 20[redacted] ECG: Bradycardia

[redacted] **20**[redacted] **HEMOGLOBIN:** 76 G/L (normal 120 to 150)

[redacted] **20**[redacted] **HEMOGLOBIN:** 101 G/L (normal 120 to 150)

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
直腸炎	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PHOCOMELIA OF LEFT UPPER EXTREMITY	20[redacted]
CROHN'S DISEASE	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 146	[redacted]20[redacted] / 146	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 197	[redacted]20[redacted] / 197	1

PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 253	[redacted]20[redacted] / 253	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 309	[redacted]20[redacted] / 309	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 365	[redacted]20[redacted] / 365	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 414	[redacted]20[redacted] / 414	1

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
NIMESULIDE	100 mg	PRN	Y-M: 20[redacted]-[redacted] / 151	ONGOING

Event #1: Serious Adverse Event

Event Description	ACUTE PARAPROCTITIS
Preferred Term	直腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 313
Age at AE Onset	1[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 313): FINGER INVESTIGATION OF RECTUM:ACUTE PARAPROCTITIS; OPENING AND DRAINAGE OF ACUTE PARAPROCTITIS:ACUTE PARAPROCTITIS

AE Stopped Rx Day	316
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CD
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]

Subject Number: [redacted]

Protocol Number: M16-000

ロシア連邦の治験責任医師からの報告。本被験者は1[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，急性直腸傍結合組織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，非飲酒者及び非喫煙者であった。

投与313日後，被験者は急性直腸傍結合組織炎を発現した。投与316日後，急性直腸傍結合組織炎は消失した。

本事象発現前，投与309日後，被験者は痔瘻（非重篤）を発現した。

投与313日後，被験者は急性肛門痛のため入院した。デジタル検査の結果，直腸傍結合組織炎が認められた。同日，被験者は急性直腸傍結合組織炎の開口及びドレナージを受けた。投与316日後，被験者は退院した。

投与された薬剤は，メトロニダゾールであった。

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) Acute proctitis (10001018) (Proctitis (10036774)) [v.23.1] [10001018]

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 PARAPROCTITIS

- Investigator: CD

- AbbVie: Event more likely related to pre-existing crohn's disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] DIGITAL INVESTIGATION OF RECTUM: acute paraproctitis

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
高窒素血症	X			
尿路結石	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	5[redacted]	MALE	WHITE

Medical History	Onset Year
BENIGN PROSTATIC HYPERPLASIA	20[redacted]
CROHN'S DISEASE	20[redacted]
KIDNEY DISORDER: AZOTEMIA	20[redacted]
OTHER: CHRONIC HEMORRHOIDS	20[redacted]
OTHER: NUTRITIONAL DEFICIENCY	20[redacted]
EYE DISEASE/DISORDER: OU CATARACT	20[redacted]
OTHER: ALOPECIA	20[redacted]
OTHER: VITILIGO	20[redacted]
OTHER: VIT D DEFICIENCY	20[redacted]
ANEMIA: NORMOCHROMIC	20[redacted]

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)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 27	[redacted]20[redacted] / 27	1

M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 51	[redacted]20[redacted] / 51	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 83	[redacted]20[redacted] / 83	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 141	[redacted]20[redacted] / 141	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 197	[redacted]20[redacted] / 197	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 238	[redacted]20[redacted] / 238	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 253	[redacted]20[redacted] / 253	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 307	[redacted]20[redacted] / 307	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 363	[redacted]20[redacted] / 363	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 420	[redacted]20[redacted] / 420	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
COLECALCIFEROL	20[redacted] OTHER: ME	QD	Y-M: 20[redacted]-[redacted] / -97

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 mg	QD	Y-M: 20[redacted]-[redacted] / 356	Y-M: 20[redacted]-[redacted] / 357
MACROGOL	64 g	TID	Y-M: 20[redacted]-[redacted] / 476	Y-M: 20[redacted]-[redacted] / 476
PROPOFOL	180 mg	QD	Y-M: 20[redacted]-[redacted] / 477	Y-M: 20[redacted]-[redacted] / 477

Event #1: Serious Adverse Event

Event Description AZOTEMIA
Preferred Term 高窒素血症
AE Onset Date / Rx Day [redacted]20[redacted] / 253
Age at AE Onset 6[redacted]
Laboratory Testing
[redacted]20[redacted] (Rx Day 436): Creatinine: 164 [72 - 115] UMOL/L; NPTST537-UREA: 11.18 [2.8 - 8.2] MMOL/L
Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 441): NEPHROBIOPSY OF LEFT KIDNEY:FOCAL ACUTE DAMAGE TO THE EPITHELIUM OF THE TUBULES. WITHOUT TUBULOINTERSTITIAL INFLAMMATION, GLOMERULOSCLEROSIS, TUBULOINTERSTITIAL FIBROSIS AND ARTERIOLOSCLEROSIS.

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

Event #2: Serious Adverse Event

Event Description	UROLITHIASIS DISEASE
Preferred Term	尿路結石
AE Onset Date / Rx Day	[redacted]20[redacted] / 388
Age at AE Onset	6[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 388): Creatinine: 161 [72 - 115] UMOL/L; NPTST537-UREA: 9.4 [2.8 - 8.2] MMOL/L

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 387): KIDNEY ULTRASOUND:RETENTION CHANGES IN THE RIGHT KIDNEY (URETERAL STRICTURE IN QUESTION); [redacted]20[redacted] (Rx Day 388): CT OF THE KIDNEYS:HYDRONEPHROTIC TRANSFORMATION OF THE RIGHT KIDNEY, IMPAIRED EXCRETORY FUNCTION OF THE RIGHT KIDNEY, CALCULUS AT THE ANTERIOR WALL OF THE BLADDER; [redacted]20[redacted] (Rx Day 391): TRANSURETHRAL ENDOSCOPIC LASER URETEROLITHO-TRYPSY:LITHO-TRYPSY; TRANSURETHRAL STENT PLACEMENT IN THE RIGHT URETER:N/A; [redacted]20[redacted] (Rx Day 435): TRANSURETHRAL STENT REMOVAL IN THE RIGHT URETER:N/A

AE Stopped Rx Day	395
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	REASON NOT ESTABLISHED.
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]

Subject Number: [redacted]

Protocol Number: M16-000

ロシア連邦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及びリサンキズマブが投与され，高窒素血症及び尿路結石症疾患の事象を発現した。

Event 1及び2の臨床経過：

関連する病歴は，良性前立腺肥大症，クローン病，慢性腎臓病，高窒素血症，栄養欠乏症，非喫煙者，非飲酒者及び尿路結石症疾患であった。

20[redacted]年[redacted]月[redacted]日，レスキュー治療としてリサンキズマブの非盲検投与が開始された。

投与253日後，被験者は高窒素血症を発現した。投与388日後，被験者は尿路結石症疾患を発現した。投与395日後，尿路結石症疾患は消失した。

投与253日後以降，クレアチニン増加（190 mm/L以下），尿素増加（13 mmol/L以下），及び高カリウム血症（6 mmol/L以下）が認められた。

投与386日後，被験者は予定された検査のため入院し，腎臓の超音波検査及びCTスキャン検査を受けた。その結果，右腎の水腎症への移行及び膀胱の前壁の結石が認められた。投与391日後，被験者は，右尿管のステント留置を伴う経尿道的内視鏡下レーザー尿管砕石術を受けた。投与395日後，被験者は退院した。

投与435日後，被験者は，右尿管の経尿道的ステント除去のため，入院した。投与441日後，診断のための腎生検が行われた。その結果，尿細管上皮に限局性急性損傷が認められたが，尿細管間質性炎症，糸球体硬化症，尿細管間質性線維症及び細動脈硬化症は認められなかった。投与442日後，被験者は退院した。

The patient's past medications include:

PREDNISOLONE for CROHN'S DISEASE ([redacted])

LOPERAMIDE for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Azotemia (10003886) (Azotaemia (10003885)) [v.23.1] [10003886]

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

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

Dechallenge: Not Applicable

2) Urolithiasis (10046707) (Calculus urinary (10007027)) [v.23.1] [10046707]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

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1) Azotemia (10003886) (Azotaemia (10003885)) [v.23.1] [10003886]

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

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

Dechallenge: Not Applicable

2) Urolithiasis (10046707) (Calculus urinary (10007027)) [v.23.1] [10046707]

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 AZOTEMIA

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing chronic kidney disease, pre-existing benign prostatic hypertrophy (BPH), and prior event of azotemia in 20[redacted].

Event of UROLITHIASIS DISEASE

- Investigator: Not reported

- AbbVie: Urolithiasis is one of the most common urological diseases in Russia, 30-40% of all patients in urological hospitals have urolithiasisis. Additionally, urolithiasis is the most common extraintestinal manifestation of crohn's disease.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of AZOTEMIA

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing chronic kidney disease, pre-existing benign prostatic hypertrophy (BPH), and prior event of azotemia in 20[redacted].

Event of UROLITHIASIS DISEASE

- Investigator: Not reported

- AbbVie: Urolithiasis is one of the most common urological diseases in Russia, 30-40% of all patients in urological hospitals have urolithiasisis. Additionally, urolithiasis is the most common extraintestinal manifestation of crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CREATININE: 190 mm/L

[redacted] **20[redacted] CREATININE:** 0.161 MMOL/L (normal 0.072 to 0.115)

[redacted] **20[redacted] CREATININE:** 0.164 MMOL/L (normal 0.072 to 0.115)

[redacted] **20[redacted] CT KIDNEYS:** Hydronephrotic transformation of the right kidney, impaired excretory function of the right kidney, calculus at the anterior wall of the bladder.

[redacted] **20[redacted] NEPHROBIOPSY OF LEFT KIDNEY:** Focal acute damage to the epithelium of the tubules. Without tubulointerstitial inflammation, glomerulosclerosis, tubulointerstitial fibrosis and arteriolosclerosis.

[redacted] 20[redacted] POTASSIUM: 6 MMOL/L

[redacted] **20[redacted] RENAL ULTRASOUND:** Retention changes in the right kidney (ureteral stricture in question)

[redacted] 20[redacted] UREA: 13 MMOL/L

[redacted] **20[redacted] UREA:** 9.4 MMOL/L (normal 2.8 to 8.2)

[redacted] **20[redacted] UREA:** 11.18 MMOL/L (normal 2.8 to 8.2)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	6[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: AXIAL ARTHROPATHY	20[redacted]
OTHER: PERIPHERAL ARTHROPATHY	20[redacted]

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	CURRENT	15 CIGARETTE	30	
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)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56	1

RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 84	[redacted]20[redacted] / 84	1

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
PARACETAMOL	1G mg	TID	Y-M: 20[redacted] / 95	Y-M: 20[redacted] / 97

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

Event Description	TERMINAL ILEUM INCOMPLETE ILEUS
Preferred Term	小腸閉塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 95 (11 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 99): Hemoglobin: 122 [130 - 170] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 95): CT ABDOMEN:OEDEMA OF THE TERMINAL ILEUM. DILATED SMALL BOWEL PROXIMALLY

AE Stopped Rx Day	102 (18 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DISEASE ASSOCIATED ILEUS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	LIFE THREATENING

Generated: [redacted]20[redacted]:09:28
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

ギリシャ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，回腸末端部不完全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，喫煙者（1 日 15 本を 30 年間）及び飲酒者（1 日 2 杯未満）であった。

投与 95 日後，被験者は回腸末端部不完全イレウスを発現した。投与 102 日後，回腸末端部不完全イレウスは消失した。

投与 95 日後，被験者はびまん性腹痛及び嘔吐のため入院した。腹部 CT 検査の結果，回腸末端部に炎症が認められた。炎症マーカーが著しく上昇していた。被験者は，鎮痛剤，ステロイド剤の静脈内投与，及び静脈内補液による保存的治療を受けた。投与 102 日後，被験者は退院した。

投与された薬剤は，Prezolon，Apotel，フラジール及び Ciproxin であった。

Causality for RISANKIZUMAB (Blinded)

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1) Partial obstruction of small intestine (10077757) (Small intestinal obstruction (10041101)) [v.23.1] [10077757]

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 TERMINAL ILEUM INCOMPLETE ILEUS

- Investigator: Disease associated ileus

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN:** Oedema of the terminal ileum. Dilated small bowel proximally.

[redacted] **20[redacted] HEMOGLOBIN:** 12.2 G/DL (normal 13 to 17)

[redacted] 20[redacted] INFLAMMATORY MARKERS: Markedly elevated

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	5[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PERIPHERAL ARTHROPATHY	NOT REPORTED
CROHN'S DISEASE	19[redacted]
INFLAMMATORY BOWEL DISEASE: ACTIVE PERIANAL DISEASE	20[redacted]
ANEMIA: IRON DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	20 CIGARETTE	42	
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)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1

M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	20[redacted] / 60	20[redacted] / 60	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 60	20[redacted] / 60	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 92	20[redacted] / 92	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 92	20[redacted] / 92	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 145	20[redacted] / 145	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 145	20[redacted] / 145	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 207	20[redacted] / 207	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 207	20[redacted] / 207	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 264	20[redacted] / 264	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 264	20[redacted] / 264	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 316	20[redacted] / 316	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 316	20[redacted] / 316	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 378	20[redacted] / 378	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 378	20[redacted] / 378	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 433	20[redacted] / 433	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 433	20[redacted] / 433	1

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
FORTRANS	SINGLE g	OTHER: SINGLE	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 460

Event #1: Serious Adverse Event

Event Description	WORSENING OF ANAEMIA
Preferred Term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 145
Age at AE Onset	5[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 145): Hematocrit: 0.22 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 64 [140 - 180] G/L;
20[redacted] (Rx Day 146): NPTST224-FERRITIN: 1 [22 - 274] NG/ML; [redacted]20[redacted] (Rx Day 148):
Hematocrit: 0.32 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 98 [140 - 180] G/L
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 145): BLOOD TRANSFUSIONS:IMPROVEMENT OF ANAEMIA

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	CHRONIC DISEASE ANAEMIA
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]

Subject Number: [redacted]

Protocol Number: M16-000

ギリシャ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，貧血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，鉄欠乏性貧血，喫煙者（1 日 20 本を 42 年間）及び非飲酒者であった。

投与 145 日後，被験者は貧血悪化を発現した。

投与 145 日後，被験者は脱力及び貧血の既往歴を訴えて入院した。ヘマトクリットが 22.3%であった。濃厚赤血球 1 単位が輸血された。入院中常に，被験者の血行動態は安定していた。投与 148 日後，被験者の状態は改善し，退院した。

投与された薬剤は，濃厚赤血球であった。

Causality for RISANKIZUMAB (Blinded)

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1) Anemia aggravated (10054309) (Anaemia (10002034)) [v.22.1] [10054309]

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 ANAEMIA

- Investigator: Chronic disease anaemia.

- AbbVie: Event is more likely related to pre-existing history of iron deficiency anemia and underlying Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ECG: normal

[redacted] **20[redacted] FERRITIN:** 1 NG/ML (normal 22 to 274)

[redacted] **20[redacted] HEMATOCRIT:** 36 % (normal 39 to 54)

[redacted] **20[redacted] HEMATOCRIT:** 34 % (normal 39 to 54)

[redacted] **20[redacted] HEMATOCRIT:** 35 % (normal 39 to 54)

[redacted] **20[redacted] HEMATOCRIT:** 32 % (normal 39 to 54)

[redacted] **20[redacted] HEMATOCRIT:** 22.3 % (normal 40 to 52)

[redacted] **20[redacted] HEMATOCRIT:** 32 % (normal 40 to 52)

[redacted] **20[redacted] HEMOGLOBIN:** 112 G/L (normal 127 to 181)

[redacted] **20[redacted] HEMOGLOBIN:** 107 G/L (normal 127 to 181)

[redacted] **20[redacted] HEMOGLOBIN:** 111 G/L (normal 127 to 181)

[redacted] **20[redacted] HEMOGLOBIN:** 101 G/L (normal 127 to 181)

[redacted] **20[redacted] HEMOGLOBIN:** 6.4 G/DL (normal 14 to 18)

[redacted] **20[redacted] HEMOGLOBIN:** 9.8 G/DL (normal 14 to 18)

[redacted] **20[redacted] MCV:** 77 FL (normal 79 to 96)

[redacted] **20[redacted] PLATELET COUNT:** 344 GI/L (normal 140 to 400)

[redacted] **20[redacted] RBC:** 4.2 TI/L (normal 4.5 to 6.4)

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
ウイルス性上気道感染	X			X

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	2[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: SINUSITIS	20[redacted]
OTHER: HERPES ZOSTER INFECTION	20[redacted]
OTHER: CORNEA EROSION OS	20[redacted]
OTHER: ABDOMINAL PAIN	20[redacted]
OTHER: FATIGUE	20[redacted]

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	FORMER	12 CIGARETTE	7	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 36	[redacted]20[redacted] / 36	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 99	[redacted]20[redacted] / 99	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 155	[redacted]20[redacted] / 155	1

PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 218	[redacted]20[redacted] / 218	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 267	[redacted]20[redacted] / 267	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	200 mg	QD	Y-M: 20[redacted]-[redacted]
VITAMINS NOS	UNKNOWN OTHER: UNKNOWN	PRN	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
VITAMINS NOS	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted]	ONGOING
DALTEPARIN	2500 IU	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 226	Y-M: 20[redacted]-[redacted] / 226
SODIUM CHLORIDE	2 L	QD	Y-M: 20[redacted]-[redacted] / 226	Y-M: 20[redacted]-[redacted] / 228
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted]-[redacted] / 226	Y-M: 20[redacted]-[redacted] / 237
PANTOPRAZOLE	40 mg	PRN	Y-M: 20[redacted]-[redacted] / 229	Y-M: 20[redacted]-[redacted] / 351

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

Event Description VIRAL UPPER RESPIRATORY INFECTION

Preferred Term ウイルス性上気道感染

AE Onset Date / Rx Day [redacted]20[redacted] / 225

Age at AE Onset 2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 226): C Reactive Protein: 16 [0 - 10] MG/L; Erythrocytes: 24 [0 - 23] /uL; Erythrocytes: 4.4 [4.5 - 5.5] 10^12/L; Hematocrit: 0.41 [0.4 - 0.5] FRACTION OF 1; Leukocytes: 12.4 [4 - 10] 10^9/L; Neutrophils: 10.17 [1.5 - 7.5] 10^9/L; Platelets: 312 [150 - 400] 10^9/L; Specific Gravity: 1.027 [1.015 - 1.025] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (Rx Day 226): OTHER THROAT SWAP RESPIRATORY VIRUSSES: Negative; [redacted]20[redacted] (Rx Day 228): STOOL BACTERIAL CAUSES: Negative; STOOL VIRAL CAUSES: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 226): VITAL SIGNS:14:28 > RR: 134/81, P: 124/MIN, TEMPERATURE: 38,7 C, RESPIRATORY FREQUENCY: 15/MIN; VITAL SIGNS:EXACT TIME UNKNOWN, BETWEEN 14:28/23:43 > T: 39.4 C.; VITAL SIGNS:23:43 > T: 37.6 (AFTER USE OF PARACETAMOL); XTHORAX:NO PATHOLOGY OF HEART OR LUNGS; [redacted]20[redacted] (Rx Day 228): VITAL SIGNS:13:02 > T=38.3 C

AE Stopped Rx Day	234
Duration of AE	10 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DECREASED IMMUNE SYSTEM POSSIBLE DUE TO USE OF AZATHIOPRIN
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

オランダ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，ウイルス性上気道感染の事象を発現した。

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 12 本を 7 年間），副鼻腔炎，腹痛，疲労及び飲酒者（1 日 2 杯未満）であった。

投与 225 日後，被験者はウイルス性上気道感染を発現した。投与 234 日後，ウイルス性上気道感染は消失した。

投与 226 日後，被験者は発熱及び咽喉痛のため入院した。入院に至るまでの数日間に，被験者は，下痢（投与 227 日後に消失），嘔吐（投与 225 日後に消失）及び腹痛（投与 227 日後に消失）も発現した。ウイルス性上気道感染と診断され，投与 228 日後，被験者は退院した。治験責任医師は，アザチオプリンが本事象のリスク因子であると判断した。本報告時点で，被験者は自宅で軽快していた。

投与された薬剤は，paracetamol，塩化ナトリウム及び dalteparin であった。

The patient's past medications include:

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

Causality for RISANKIZUMAB (Blinded)

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1) Viral upper respiratory tract infection (10047482) (Viral upper respiratory tract infection (10047482)) [v.24.0] [10047482]

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 VIRAL UPPER RESPIRATORY INFECTION

- Investigator: DECREASED IMMUNE SYSTEM POSSIBLE DUE TO USE OF AZATHIOPRIN

- AbbVie: Event is common in the general population this time of year.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BODY TEMPERATURE: 39.4 Degrees C

[redacted] 20[redacted] BODY TEMPERATURE: 37.6 Degrees C

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

[redacted] **20[redacted] CRP:** 16 MG/L (normal 0 to 10)

[redacted] **20[redacted] HEMATOCRIT:** 0.41 I/I (normal 0.4 to 0.5)

[redacted] **20[redacted] NEUTROPHILS ABS:** 10.17 X10**9/L (normal 1.5 to 7.5)

[redacted] **20[redacted] PLATELET COUNT:** 312 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.38 X10**12/L (normal 4.5 to 5.5)

[redacted] **20[redacted] SPECIFIC GRAVITY:** 1.027 no unit (normal 1.015 to 1.025)

[redacted] **20[redacted] STOOL:** viral causes- negative; bacterial causes- negative

[redacted] **20[redacted] THROAT SWAB:** Negative for respiratory viruses

[redacted] 20[redacted] URINE RED BLOOD CELLS: 24 MCL (normal 0 to 23)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 12.4 X10**9/L (normal 4.0 to 10.0)

[redacted] **20[redacted] X-RAY THORAX:** No pathology of heart or lungs

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			
胃腸吻合部狭窄	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	3[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
INFLAMMATORY BOWEL DISEASE: ANASTOMOTIC ABSCESS	20
INFLAMMATORY BOWEL DISEASE: INTESTINAL SUBOCCLUSION	20
OTHER: INTERMITTENT PERIPHERAL ARTHROPATHY	20
OTHER: FATIGUE	20
GASTROESOPHAGEAL REFLUX DISEASE	20
OTHER: INTERMITTENT DIZZINESS	20
OTHER: INTERMITTENT ABDOMINAL PAIN	20
OTHER: INTERMITTENT NAUSEA	20
OTHER: INTERMITTENT SLEEPING DISORDERS	20
OTHER: INTERMITTENT VOMITING	20
GASTROESOPHAGEAL REFLUX DISEASE	20

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF ABDOMINAL ABSCESS	20
CROHN'S DISEASE SURGICAL HISTORY: ILEOSTOMY CLOSING	20
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	20
CROHN'S DISEASE HISTORY: COLONOSCOPY	20

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)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 32	[redacted]20[redacted] / 32	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 93	[redacted]20[redacted] / 93	1
M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 93	[redacted]20[redacted] / 93	1
M15991 /RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 93	[redacted]20[redacted] / 93	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 120	[redacted]20[redacted] / 120	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 148	[redacted]20[redacted] / 148	1
M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 148	[redacted]20[redacted] / 148	1
M15991 /RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 148	[redacted]20[redacted] / 148	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 171	[redacted]20[redacted] / 171	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 171	[redacted]20[redacted] / 171	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 227	[redacted]20[redacted] / 227	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 227	[redacted]20[redacted] / 227	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 285	[redacted]20[redacted] / 285	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 285	[redacted]20[redacted] / 285	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 337	[redacted]20[redacted] / 337	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 337	[redacted]20[redacted] / 337	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] / 466	[redacted]20[redacted] / 466	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 466	[redacted]20[redacted] / 466	1

PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 544	[redacted]20[redacted] / 544	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 544	[redacted]20[redacted] / 544	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 955	[redacted]20[redacted] / 955	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
INFLIXIMAB	5 mg/kg	OTHER: INDUCTION PHASE (DOSING 0,2,6 WEEKS)	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	160 mg	OTHER: ONE 160 MG SC DOSE AT WEEK 0.	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: ONE 80 MG SC DOSE AT WEEK 2	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	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
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -7	NOT REPORTED
ALPRAZOLAM	0.5 mg	PRN	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 544
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 400	ONGOING
ALIZAPRIDE	50 mg	QD	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 444
PARACETAMOL	1 g	QD	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 444
TRAMADOL	100 mg	QD	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 444
PERDOLAN	1 g	PRN	Y-M: 20[redacted] / 446	Y-M: 20[redacted] / 448
IRON	525 mg	QD	Y-M: 20[redacted] / 449	NOT REPORTED

ALIZAPRIDE	50 mg	QD	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
TRAMADOL	100 mg	QD	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 465
HYOSCINE	10 mg	QD	Y-M: 20[redacted] / 464	Y-M: 20[redacted] / 465
OSMOTICALLY ACTING LAXATIVES	4 L	PRN	Y-M: 20[redacted] / 464	Y-M: 20[redacted] / 465
PROPOFOL	1 %	PRN	Y-M: 20[redacted] / 465	Y-M: 20[redacted] / 465

Event #1: Serious Adverse Event

Event Description	CROHN DISEASE FLARE
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 444
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day -2479): Hemoglobin: 97 [130 - 180] G/L; [redacted]20[redacted] (Rx Day 444): C Reactive Protein: 2.6 [NOT REPORTED - 5] mg/L; Hematocrit: 0.35 [0.4 - 0.53] FRACTION OF 1; Neutrophils/Leukocytes: 84.5 [40 - 75] %; [redacted]20[redacted] (Rx Day 446): C Reactive Protein: 21 [NOT REPORTED - 5] mg/L; [redacted]20[redacted] (Rx Day 447): NPTST103-CALPROTECTINE: 623 [50 - NOT REPORTED] MICRO GRAMME/GRAMME; [redacted]20[redacted] (Rx Day 449): C Reactive Protein: 3.4 [NOT REPORTED - 5] mg/L; Hematocrit: 0.33 [0.4 - 0.53] FRACTION OF 1; Hemoglobin: 91 [130 - 180] G/L

Microbiology

[redacted]20[redacted] (Rx Day 447): STOOL CLOSTRIDIUM DIFFICILE SCREENIIN: Negative; STOOL ENTEROPATHOGEN DETECTION: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 444): CT SCAN ABDOMINAL:NO OCCLUSION DETECTED NO EVIDENCE FOR AN ACUTE FLARE OF THE CROHN DISEASE

AE Stopped Rx Day	449
Duration of AE	6 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN DISEASE UNCONTROLLED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	FIBROTIC SUBSTENOSIS AT THE ILEO-COLIC ANASTOMOSIS
Preferred Term	胃腸吻合部狭窄
AE Onset Date / Rx Day	[redacted]20[redacted] / 453

Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day -2469): Hemoglobin: 92 [130 - 180] G/L; [redacted]20[redacted] (Rx Day 454): C Reactive Protein: 11 [5 - NOT REPORTED] mg/L; Hematocrit: 0.33 [0.4 - 0.53] FRACTION OF 1; [redacted]20[redacted] (Rx Day 457): C Reactive Protein: 1.7 [5 - NOT REPORTED] mg/L; Hemoglobin: 96 [130 - 180] G/L

Microbiology

[redacted]20[redacted] (Rx Day 457): STOOL CLOSTRIDIUM DIFFICILE SCRRENING: Positive-TOXINE A/B : POSITIVE

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 453): CT ABDOMINAL SCAN:BOWEL OCCLUSION WITH PROBABLY A ILEOCOLIC STENOSIS; STOMACH FLUID ASPIRATION WITH NASO GASTRIC TUBE:NOT APPLICABLE; [redacted]20[redacted] (Rx Day 458): CT SCAN ABDOMINAL:FIBROTIC SUBSTENONIS; [redacted]20[redacted] (Rx Day 494): COLONOSCOPY FOR COLIC DILATATION:DILATED STENOSIS

AE Stopped Rx Day	494
Duration of AE	42 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated:[redacted]20[redacted]:09:28
Program Source Code:[redacted]

Investigator No.:[redacted]

Subject Number:[redacted]

Protocol Number: M16-000

ベルギー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，クローン病のフレアの事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，吻合部膿瘍，腸管亜閉塞，間欠性末梢性関節障害，間欠性腹痛，間欠性浮動性めまい，間欠性悪心，間欠性嘔吐，胃食道逆流性疾患，非喫煙者及び非飲酒者であった。

投与 444 日後，被験者はクローン病のフレアを発現した。投与 449 日後，クローン病のフレアは消失した。

投与 444 日後，被験者は入院した。血液培養の結果は陰性であり，CT 検査の結果，閉塞や急性フレアの徴候は認められなかった。入院中，被験者は鎮痛剤の投与を受け，症状は改善した。投与 449 日後，被験者は退院した。

投与された薬剤は，Perfusalgan，アセトアミノフェン，Litican，Tradonal，Perdolan 及び Fero-Gradumet であった。

The patient's past medications include:

INFLIXIMAB for CROHN'S DISEASE ([redacted])

ADALIMUMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Crohns disease aggravated (10011408) (Crohn's disease (10011401)) [v.23.0] [10011408]

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 CROHN DISEASE FLARE

- **Investigator:** CROHN DISEASE UNCONTROLLED

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL CT:** No occlusion detected; no evidence of an acute flare of crohn's disease

[redacted] CALPROTECTINE: 623 MCG (normal >50)

[redacted] **20[redacted] HCT:** 34.7 % (normal 40 to 53)

[redacted] 20[redacted] HEMATOCRIT: 0.41 no units

[redacted] 20[redacted] HEMATOCRIT: 0.44 no units

[redacted] 20[redacted] HEMATOCRIT: 0.39 no units

[redacted] 20[redacted] HEMATOCRIT: 0.35 no units

[redacted] 20[redacted] HEMATOCRIT: 0.35 no units

[redacted] **20[redacted] HEMATOCRIT:** 32.7 % (normal 40 to 53)

[redacted] 20[redacted] HEMOGLOBIN: 126 G/L

[redacted] 20[redacted] HEMOGLOBIN: 142 G/L

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

[redacted] 20[redacted] HEMOGLOBIN: 111 G/L

[redacted] 20[redacted] HEMOGLOBIN: 104 G/L

[redacted] **20[redacted] HEMOGLOBIN:** 9.1 G/DL (normal 13 to 18)

[redacted] **20[redacted] HGB:** 9.7 G/DL (normal 13 to 18)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 2.6 mg/dL (normal < 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 21 mg/dL (normal < 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 3.4 mg/dL (normal < 5)

[redacted] **20[redacted] NEUTROPHILS:** 84.5 % (normal 40 to 75)

[redacted] 20[redacted] STOOL C- DIFF: Negative

[redacted] 20[redacted] STOOL ENTEROPATHOGENS: Negative

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

ベルギー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，回結腸吻合部の線維性亜狭窄の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，クローン病，腸切除，腹部膿瘍ドレナージ，炎症性腸疾患（吻合部膿瘍），回腸瘻造設の閉鎖，炎症性腸疾患（腸管亜閉塞），腸切除，瘻孔切開，間欠性腹痛，間欠性悪心，間欠性嘔吐，胃食道逆流性疾患，非喫煙者及び非飲酒者であった。

投与 453 日後，被験者は回結腸吻合部の線維性亜狭窄を発現した。投与 494 日後，回結腸吻合部の線維性亜狭窄は消失した。

投与 453 日後，被験者は急性腹痛，嘔吐，悪心及び下痢のため入院した。便検査の結果，クロストリジウム・ディフィシレが陽性であった。被験者は胃液の誤嚥に対して経鼻胃管の留置を受けた。投与 460 日後，被験者は退院した。投与 494 日後，被験者は結腸内視鏡検査及び狭窄拡張術を受けた

投与された薬剤は，クレキサン，メドロール，Litican，Tradonal，paracetamol 及びフラジールであった。

The patient's past medications include:

INFLIXIMAB for CROHN'S DISEASE ([redacted])

ADALIMUMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Gastrointestinal anastomotic stenosis (10078817) (Gastrointestinal anastomotic stenosis (10078817)) [v.23.0] [10078817]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of FIBROTIC SUBSTENOSIS AT THE ILEO-COLIC ANASTOMOSIS

- Investigator: Not applicable

- AbbVie: Event is more likely related to pre-existing Crohn's disease and prior surgeries for crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CLOSTRIDIUM DIFFICILE SCREENING: Toxine A/B: Positive

[redacted] 20[redacted] COLONOSCOPY: Stenosis dilation

[redacted] **20[redacted] CT ABDOMEN:** bowel occlusion with probable ileo-colic stenosis

[redacted] **20[redacted] CT ABDOMEN:** Fibrotic substenosis at the ileo-colic anastomosis

[redacted] **20[redacted] HCT:** 32.8 % (normal 40 to 53)

[redacted] **20[redacted] HGB:** 9.6 G/DL (normal 13 to 18)

[redacted] 20[redacted] HIGH SENSITIVITY CRP: 1.7 MG/L (normal >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
腹痛	X			
腹膜垂炎	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	3[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: SINGLE TESTICLE	19[redacted]
ASTHMA	19[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: PENTASA ALLERGIA	20[redacted]
OTHER: ORAL APHTOSIS	20[redacted]
OTHER: MODERATE ARTHRALGIA	20[redacted]
OTHER: MODERATE ASTHENIA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: AMYGDALECTOMIA	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64	1

PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 86 86	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 134 134	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 198 198	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 251 251	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 310 310	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 366 366	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 422 422	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BETAMETHASONE	1 DF	QD	Y-M: 20[redacted]-[redacted] / 15
LOPERAMIDE	2 OTHER: CAPS	QD	Y-M: 20[redacted]-[redacted] / 65

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
PICO-SALAX	2 DF	PRN	Y-M: 20[redacted]-[redacted] / 454	Y-M: 20[redacted]-[redacted] / 455

Event #1: Serious Adverse Event

Event Description EPIPLOID APPENDIX
Preferred Term 腹膜垂炎
AE Onset Date / Rx Day [redacted]20[redacted] / 478 (56 DAYS AFTER LAST TREATMENT)
Age at AE Onset 3[redacted]
Laboratory Testing
[redacted]20[redacted] (Rx Day 484): C Reactive Protein: 11 [11 - 11] MG/L
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 475): CEALIOSCOPY EXPLORATION:EPIPLOID APPENDIX; [redacted]20[redacted] (Rx Day 477): ABDOMINAL CT SCAN:EPIPLOID APPENDIX
AE Stopped Rx Day 479 (57 DAYS AFTER LAST TREATMENT)
Duration of AE 2 DAYS
Severity MODERATE
Relation to Study Drug by Investigator No Reasonable Possibility
Investigator Alternative Etiology EPIPLOID APPENDIX

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

Event #2: Serious Adverse Event

Event Description	ABDOMINAL PAIN EXACERBATION
Preferred Term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 479 (57 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 484): PELVIEN ABDOMINAL SCANNER:NO CLINICAL RESULT FOUND

AE Stopped Rx Day	487 (65 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN DISEASE EXACERBATION
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

フランス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及びリサンキズマブが投与され，腹膜垂炎及び腹痛増悪の事象を発現した。

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 1 箱を 9 年間），口腔内アフタ症及び飲酒者（1 日 2 杯未満）であった。

20[redacted]年[redacted]月[redacted]日，レスキュー治療としてリサンキズマブの非盲検投与が開始された。

投与 478 日後，被験者は腹膜垂炎を発現した。投与 479 日後，被験者は腹痛増悪を発現した。投与 479 日後，腹膜垂炎は消失した。投与 487 日後，腹痛増悪は消失した。

投与 477 日後，被験者は腸骨窩腹痛のため入院した。被験者は腹腔鏡検査による診査を受けた。投与 479 日後，被験者は退院した。

投与 481 日後，被験者は腹痛増悪のため入院した。投与 487 日後，被験者は退院した。

投与された薬剤は，オーグメンチン及び Solupred であった。

The patient's past medications include:

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

Causality for RISANKIZUMAB (Blinded)

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1) Epiploic appendagitis (10064231) (Epiploic appendagitis (10064231)) [v.23.1] [10064231]

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

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

Dechallenge: Not Applicable

2) Abdominal pain aggravated (10048358) (Abdominal pain (10000081)) [v.23.1] [10048358]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

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1) Epiploic appendagitis (10064231) (Epiploic appendagitis (10064231)) [v.23.1] [10064231]

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

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

Dechallenge: Not Applicable

2) Abdominal pain aggravated (10048358) (Abdominal pain (10000081)) [v.23.1] [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 EPIPLOIC APPENDIX

- Investigator: EPIPLOID APPENDIX

- AbbVie: Event not consistent with study drug's mechanism of action. Epiploic appendagitis is an ischemic infarction of an epiploic appendage caused by torsion or spontaneous thrombosis of the epiploic appendage central draining vein.

Event of ABDOMINAL PAIN EXACERBATION

- Investigator: CROHN DISEASE EXACERBATION

- AbbVie: Event is more likely related to concurrent epiploic appendagitis. Additional risk factor includes pre-existing Crohn's disease.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of EPIPLOIC APPENDIX

- Investigator: EPIPLOID APPENDIX

- AbbVie: Event not consistent with study drug's mechanism of action. Epiploic appendagitis is an ischemic infarction of an epiploic appendage caused by torsion or spontaneous thrombosis of the epiploic appendage central draining vein.

Event of ABDOMINAL PAIN EXACERBATION

- Investigator: CROHN DISEASE EXACERBATION

- AbbVie: Event is more likely related to concurrent epiploic appendagitis. Additional risk factor includes pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL CT SCAN: EPIPLOIC APPENDIX

[redacted] 20[redacted] CEALIOSCOPY: EPIPLOID APPENDIX

[redacted] **20[redacted] CRP:** 11 MG/L (normal <11)

[redacted] 20[redacted] PELVIS/ABDOMINAL CT SCAN: No clinical result found

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			
高体温症	X	X		
腹膜炎	X			X
亜イレウス	X	X		

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: PSORIASIS	20
OTHER: RECURRENT BRONCHITIS	20
OTHER: LOSS OF APPETITE	20
OTHER: MODERATE ARTHRALGIA	20
OTHER: NAUSEA	20
OTHER: IMPLANT FOR CONTRACEPTION	20

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: ILEO COLONIC RESECTION	20
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20
SURGERY: CAESAREAN	20
CROHN'S DISEASE HISTORY: COLONOSCOPY	20
SURGERY: CAESAREAN	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	UNKNOWN			
CIGARETTES	FORMER	10 CIGARETTE	15	19[redacted]
CIGARS	UNKNOWN			
E-CIGARETTES	CURRENT	10 SESSIONS	23	
PIPES	UNKNOWN			

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)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 28	[redacted] / 28	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 28	[redacted] / 28	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 56	[redacted] / 56	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 56	[redacted] / 56	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 83	[redacted] / 83	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 146	[redacted] / 146	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 191	[redacted] / 191	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 252	[redacted] / 252	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: 19[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -286
HORMONAL CONTRACEPTIVES FOR SYSTEMIC USE	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / -166

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
HORMONAL CONTRACEPTIVES FOR SYSTEMIC USE	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / -166	ONGOING
PARACETAMOL	3 g	QD	Y-M: 20[redacted] / 333	Y-M: 20[redacted] / 334
PIPERACILLIN	4 g	OTHER: ONCE	Y-M: 20[redacted] / 334	Y-M: 20[redacted] / 334
TAZOBACTAM	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 334	Y-M: 20[redacted] / 334

Event #1: Serious Adverse Event

Event Description	FLARE OF CROHN DISEASE
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 181
Age at AE Onset	3[redacted]
Laboratory Testing	
[redacted]20[redacted] (Rx Day 189): Hematocrit: 0.4 [0.36 - 0.4] FRACTION OF 1	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx Day 188): ABDOMINAL PELVIC SCANNER:ABSENCE OF NEW HAEMIC STENOSIS DEMONSTRATED	
AE Stopped Rx Day	183
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ILEAL STENOSIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	PERITONITIS
Preferred Term	腹膜炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 277 (25 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	308 (56 DAYS AFTER LAST TREATMENT)
Duration of AE	32 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	RELATED TO CROHN DESEASE. NONE OTHER CAUSE DEFINED.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	SUB-OCCLUSIVE SYNDROME
Preferred Term	亜イレウス

AE Onset Date / Rx Day	[redacted]20[redacted] / 277 (25 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
[redacted]20[redacted] (Rx Day 277): Hemoglobin: 112 [82 - 112] G/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx Day 277): CT-SCAN:PERITONEAL EFFUSION; SURGERY:ILEOSTOMIA	
AE Stopped Rx Day	308 (56 DAYS AFTER LAST TREATMENT)
Duration of AE	32 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PERITONITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

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

Event Description	HYPERTHERMIA
Preferred Term	高体温症
AE Onset Date / Rx Day	[redacted]20[redacted] / 333 (81 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
[redacted]20[redacted] (Rx Day 333): C Reactive Protein: 14 [5 - 14] MG/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx Day 333): ABDOMINO-PELVIC SCANNER:NO SMALL BOWEL STENONIS	
AE Stopped Rx Day	334 (82 DAYS AFTER LAST TREATMENT)
Duration of AE	2 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INTRAPERITONEAL FISTULA IN LEFT ILIAC FOSSA
Discontinued Study Drug Due to the Event	YES
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

フランス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，クローン病のフレアの事象を発現した。

Event 1の臨床経過：

関連する病歴は，元喫煙者（1日10本を23年間），回腸結腸切除，腸切除，食欲喪失，中等度の関節痛，悪心，クローン病，電子タバコ使用者（1日10回を23年間）及び禁酒であった。その他の併用療法は避妊インプラント（20[redacted]年[redacted]月～現在）であった。

投与181日後，被験者はクローン病のフレアを発現した。投与183日後，クローン病のフレアは消失した。

投与181日後，被験者は腹痛のため入院した。被験者は回復し，本事象は消失した。投与183日後，被験者は退院した。

投与された薬剤は，プレドニゾロンであった。

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 FLARE OF CROHN DISEASE

- Investigator: ILEAL STENOSIS

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ABDOMINAL PELVIC SCANNER:** DISTENSION OF THE RIGHT COLON UPSTREAM OF THE ILEO-CAECAL ANASTOMOSIS. STABILITY OF THE INFLAMMATORY ASPECT OF THE TERMINAL ILEUM. ABSENCE OF NEW HAEMIC STENOSIS DEMONSTRATED

[redacted] 20[redacted] **ABDOMINAL PELVIC SCANNER:** ABSENCE OF NEW HAEMIC STENOSIS DEMONSTRATED

[redacted] 20[redacted] **HEMATOCRIT:** 40 % (normal 36 to 40)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

フランス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，亜閉塞症候群及び腹膜炎の事象を発現した。

Event 2 及び 3 の臨床経過：

関連する病歴は，元喫煙者（1 日 10 本を 15 年間），クローン病及び非飲酒者であった。その他の併用療法は避妊インプラントであった。

投与 277 日後，被験者は亜閉塞症候群及び腹膜炎を発現した。投与 308 日後，亜閉塞症候群及び腹膜炎は消失した。

投与 277 日後，被験者は亜閉塞症候群によるあられのような穿孔のため入院した。同日，被験者は回腸瘻造設を受けた。本事象の臨床経過には，「砂利のような穿孔」による多臓器不全を伴う敗血症性ショックが含まれていた。投与 308 日後，被験者は退院した。

亜閉塞症候群の事象により治験薬の投与が完全に中止された。

投与された薬剤は，Amikacine 及び Tazocilline であった。

The patient's past medications include:

PREDNISOLONE for ABDOMINAL PAIN and CROHN'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Subocclusive syndrome (10059670) (Subileus (10050396)) [v.24.0] [10059670]

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

2) Peritonitis (10034674) (Peritonitis (10034674)) [v.24.0] [10034674]

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 SUB-OCCLUSIVE SYNDROME

- Investigator: Peritonitis

- AbbVie: Risk factors include pre-existing Crohn's Disease

Event of PERITONITIS

- Investigator: Related to Crohn disease. None other cause defined.

- AbbVie: Risk factors include pre-existing Crohn's Disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT SCAN:** Peritoneal effusion

[redacted] **20[redacted] HEMOGLOBIN:** 11.2 G/L (normal 8.2 to 11.2)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

フランス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，高体温症の事象を発現した。

Event 4の臨床経過：

関連する病歴は，元喫煙者，クローン病，腸切除，回腸結腸切除，非飲酒者及び電子タバコ喫煙者（1日10回）であった。

投与333日後，被験者は高体温症を発現した。投与334日後，高体温症は消失した。

本事象発現前，治験薬の投与が完全に中止された。

投与333日後，被験者は高体温症の症状のため入院した。腹腔内膿孔が左腸骨窩に認められ，また歯肉膿孔の可能性も認められた。虚脱状態の腹腔内左腸骨窩に放射線ドレーンが留置された。投与334日後，被験者は退院した。

投与された薬剤は，タゾバクタム，paracetamol及びPiperacillineであった。

The patient's past medications include:

PREDNISOLONE for ABDOMINAL PAIN ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Hyperthermia (10020843) (Hyperthermia (10020843)) [v.23.1] [10020843]

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 HYPERTHERMIA

- Investigator: INTRAPERITONEAL FISTULA IN LEFT ILIAC FOSSA

- AbbVie: Risk factors include intraperitoneal fistula in left iliac fossa as noted by PI and pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINO-PELVIC SCANNER: No bowel stenosis

[redacted] **20[redacted] CRP:** 14 MG/L (normal >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
関節炎	X			
背部痛	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]

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)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 82	[redacted]20[redacted] / 82	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 168	[redacted]20[redacted] / 168	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 201	[redacted]20[redacted] / 201	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 257	[redacted]20[redacted] / 257	1

RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 320	[redacted]20[redacted] / 320	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 364	[redacted]20[redacted] / 364	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 418	[redacted]20[redacted] / 418	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
INTRAUTERINE CONTRACEPTIVE DEVICE	NON APPLICABLE OTHER: NON APPLICABLE	OTHER: NON APPLICABLE	Y-M: 20[redacted]
INTRAUTERINE CONTRACEPTIVE DEVICE	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted]-[redacted] / -47

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
INTRAUTERINE CONTRACEPTIVE DEVICE	NON APPLICABLE OTHER: NON APPLICABLE	OTHER: NON APPLICABLE	Y-M: 20[redacted]	ONGOING
INTRAUTERINE CONTRACEPTIVE DEVICE	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted]-[redacted] / -47	ONGOING
COLCHICINE	1 mg	QD	Y-M: 20[redacted]-[redacted] / 151	Y-M: 20[redacted]-[redacted] / 165
OXAZEPAM	20 mg	QD	Y-M: 20[redacted]-[redacted] / 165	ONGOING
PARACETAMOL	3 g	QD	Y-M: 20[redacted]-[redacted] / 165	ONGOING
PREGABALIN	3 g	QD	Y-M: 20[redacted]-[redacted] / 165	ONGOING

Event #1: Serious Adverse Event

Event Description ACUTE BACK PAIN
Preferred Term 背部痛
AE Onset Date / Rx Day [redacted]20[redacted] / 142
Age at AE Onset 4[redacted]
Laboratory Testing
[redacted]20[redacted] (Rx Day 142): C Reactive Protein: 3.6 [3.6 - 3.6] MG/L
Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 144): MRI OF RACHIS:BACK PAIN DUE TO INFLAMMATORY INVOLVEMENT OF THE SPINE, POSSIBLY LINKED TO THE CROHN'S DISEASE AND LOW BACK PAIN ON SPONDYLOLISTESIS (L4-L5) WITH OPERATIVE INDICATION

AE Stopped Rx Day	152
Duration of AE	11 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	LOMBALGIA INFLAMMATORY INVOLVEMENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	ARTHRITIS OF LEFT KNEE
Preferred Term	関節炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 160
Age at AE Onset	4[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 160): C Reactive Protein: 102 [19 - 19] MG/L

Microbiology
[redacted]20[redacted] (Rx Day 161): OTHER KNEE PUNCTURE KNEE PUNCTURE: Negative

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 161): PONCTURE OF LEFT KNEE:INFLAMMATORY RHUMATISM BEGINNER CHORINIC WITH PERIPHERAL MANIFESTATION

AE Stopped Rx Day	165
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INFLAMMATORY RHUMATISM BEGINNER CHORINIC WITH PERIPHERAL MANIFESTATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	ACUTE DORSALGIA
Preferred Term	背部痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 160
Age at AE Onset	4[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 160): C Reactive Protein: 102 [19 - 19] MG/L

Microbiology
[redacted]20[redacted] (Rx Day 161): OTHER KNEE PUNCTURE KNEE PUNCTURE: Negative

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 161): PONCTURE OF LEFT KNEE:INFLAMMATORY RHUMATISM BEGINNER CHORINIC WITH PERIPHERAL MANIFESTATION

AE Stopped Rx Day	165
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INFLAMMATORY RHUMATISM BEGINNER CHORINIC WITH PERIPHERAL MANIFESTATION
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

フランス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，急性背部痛の事象を発現した。

Event 1 の臨床経過：
関連する病歴は，クローン病，変形性関節症，子宮内避妊具，非喫煙者及び非飲酒者であった。

投与 142 日後，被験者は急性背部痛を発現した。投与 152 日後，急性背部痛は消失した。

投与 142 日後，被験者は重度の肋間神経痛のため入院した。投与 152 日後，被験者は退院した。

投与された薬剤は，オキサゼパム，paracetamol，Pregabaline 及びコルヒチンであった。

The patient's past medications include:

IMUREL for UNKNOWN INDICATION

Causality for RISANKIZUMAB (Blinded)

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1) Acute back pain (10000683) (Back pain (10003988)) [v.23.1] [10000683]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of ACUTE BACK PAIN

- Investigator: Lombalgia inflammatory involvement.

- AbbVie: Event more likely related to arthritic manifestations of underlying Crohn's disease. Additional risk factor is pre-existing Osteoarthritis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 3.6 MG/L (normal <3.6)

[redacted] **20[redacted] MRI OF RACHIS:** BACK PAIN DUE TO INFLAMMATORY INVOLVEMENT OF THE SPINE, POSSIBLY LINKED TO THE CROHN'S DISEASE AND LOW BACK PAIN ON SPONDYLOLISTESIS (L4-L5) WITH OPERATIVE INDICATION

[redacted] 20[redacted] WEIGHT: 6[redacted] KG

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

フランス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，左膝関節炎及び急性背部痛の事象を発現した。

Event 2 及び 3 の臨床経過：

関連する病歴は，クローン病，変形性関節症，非喫煙者及び非飲酒者であった。

投与 160 日後，被験者は左膝関節炎及び急性背部痛を発現した。投与 165 日後，左膝関節炎及び急性背部痛は消失した。

本事象発現前の投与 142 日後，被験者は急性背部痛のため入院した（AER [redacted]）。

投与 160 日後，被験者は左膝痛及び背部痛のため入院した。投与 161 日後，被験者は左膝の穿刺を受けた。その結果，末梢性症状を伴う，慢性初期の炎症性リウマチが認められた。投与 165 日後，被験者は退院した。

投与された薬剤は，オキサゼパム，paracetamol 及び Pregabaline であった。

Causality for RISANKIZUMAB (Blinded)

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1) Knee arthritis (10067624) (Arthritis (10003246)) [v.23.1] [10067624]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

2) Acute back pain (10000683) (Back pain (10003988)) [v.23.1] [10000683]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of ARTHITIS OF LEFT KNEE

- Investigator: Inflammatory rheumatism beginner chronic with peripheral manifestation.

- AbbVie: Event is more likely related to pre-existing osteoarthritis and crohn's disease.

Event of ACUTE DORSALGIA

- Investigator: Inflammatory rheumatism beginner chronic with peripheral manifestation.

- AbbVie: Event is more likely related to pre-existing osteoarthritis and crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 102 MG/L (normal 19 to 19)

[redacted] **20[redacted] PUNCTURE OF LEFT KNEE- FLUID ANALYSIS:** INFLAMMATORY RHUMATISM BEGINNER CHORINIC WITH PERIPHERAL MANIFESTATION

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
ウイルス感染	X			X

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	3[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: INFLIXIMAB-INDUCED PSORIASIS	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF ANAL ABSCESS	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 113	[redacted]20[redacted] / 113	1

M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 134	[redacted]20[redacted] / 134	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 134	[redacted]20[redacted] / 134	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 173	[redacted]20[redacted] / 173	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 230	[redacted]20[redacted] / 230	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 286	[redacted]20[redacted] / 286	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 343	[redacted]20[redacted] / 343	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 398	[redacted]20[redacted] / 398	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 411	[redacted]20[redacted] / 411	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 456	[redacted]20[redacted] / 456	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 516	[redacted]20[redacted] / 516	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]-[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
NOT REPORTED				

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

Event Description VIRAL INFECTION

Preferred Term ウイルス感染

AE Onset Date / Rx Day [redacted]20[redacted] / 340

Age at AE Onset 3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 337): C Reactive Protein: 84.6 [NOT REPORTED - 5] mg/L; NPTST125-CMV: NOT DETECTED [NOT REPORTED - NOT REPORTED] NOT APPLICABLE

Microbiology

[redacted]20[redacted] (Rx Day 337): STOOL CLOSTRIDIUM DIFFICILE: Negative; [redacted]20[redacted] (Rx Day 340): OTHER NASAL SWAB COVID-19 DIAGNOSTIC TEST: Negative; [redacted]20[redacted] (Rx Day 341): URINE CYTOBACTERIOGICAL TESTING: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 341): CHEST RADIOGRAPHY:NORMAL

AE Stopped Rx Day 342

Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:09:28
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

フランス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，ウイルス感染の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，手術（肛門膿瘍のドレナージ），非喫煙者及び非飲酒者であった。

投与 340 日後，被験者はウイルス感染を発現した。投与 342 日後，ウイルス感染は消失した。

投与 328 日後以降，被験者は，液状血便の増加，寝汗及び著しい無力症を発現していた。投与 337 日後，CRP が測定された結果，84.6 mg/L であり，便検査の結果，クロストリジウム・ディフィシレは陰性であった。

投与 340 日後，被験者はウイルス感染，発熱，及び排便回数増加のため入院した。COVID-19 用鼻腔スワブ検査の結果は陰性であった。投与 341 日後，検尿の結果も陰性であった。被験者は自然に改善し，投与 342 日後，退院した。

The patient's past medications include:

INFLIXIMAB for CROHN'S DISEASE

Causality for RISANKIZUMAB (Blinded)

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1) Viral infection (10047461) (Viral infection (10047461)) [v.23.1] [10047461]

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 VIRAL INFECTION

- Investigator: infection

- AbbVie: Viral infections occur commonly in the general population. Additionally, subject's infectious disease diagnostic work up was negative.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CHEST RADIOGRAPHY: Normal

[redacted] **20[redacted] CMV:** None detected

[redacted] **20[redacted] CRP:** 84.6 MG/L (normal <5)

[redacted] 20[redacted] NASAL SWAB FOR COVID-19: Negative

[redacted] **20[redacted] STOOL ANALYSIS:** Negative for clostridium difficile

[redacted] 20[redacted] URINALYSIS: Negative

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	4[redacted]	MALE	WHITE

Medical History	Onset Year
LATENT TUBERCULOSIS	NOT REPORTED
OTHER: INFECTION LATENT TUBERCULOSIS	NOT REPORTED
INFLAMMATORY BOWEL DISEASE: DIARRHEA	20[redacted]
CROHN'S DISEASE	20
OTHER: PERIPHERAL ARTHROPATHY	20
OTHER: ASTHENIE	20
INFLAMMATORY BOWEL DISEASE: ABDOMINAL PAIN	20
MIGRAINE HEADACHE: CHRONIC HEADACHE	20
INFLAMMATORY BOWEL DISEASE: ANAL PRURITUS	20
OTHER: ACNE ON THE FACE	20
OTHER: AXIAL ARTHROPATHY	20
OTHER: INCREASE PERIPHERAL ARTICULAR PAIN	20

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: ILEO-CAECALE	20
CROHN'S DISEASE HISTORY: COLONOSCOPY	20

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)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 31	[redacted] / 31	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 64	[redacted] / 64	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 91	[redacted] / 91	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 148	[redacted] / 148	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted] / 207	[redacted] / 207	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 262	[redacted] / 262	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 317	[redacted] / 317	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
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted] / 464	[redacted] / 464	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
PREDNISOLONE	15 mg	OTHER: ONCE	Y-M: 20[redacted] / -52
PARACETAMOL	1 g	OTHER: AS NEEDED	Y-M: 20[redacted] / 15
PARACETAMOL	1000 mg	OTHER: AS NECESSARY	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
PARACETAMOL	1 g	OTHER: AS NEEDED	Y-M: 20[redacted] / 15	NOT REPORTED
ESOMEPRAZOLE	40 mg	OTHER: AS NEEDED	Y-M: 20[redacted] / 248	NOT REPORTED
PAPAVER SOMNIFERUM W/PARACETAMOL	500/25 mg	OTHER: AS NECESSARY	Y-M: 20[redacted] / 416	ONGOING
AMITRIPTYLINE	12.5 mg	QD	Y-M: 20[redacted] / 416	Y-M: 20[redacted] / 420

Event #1: Serious Adverse Event

Event Description	AXIAL AND PERIPHERAL ARTHROPATHY
Preferred Term	関節障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 416
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (Rx Day 417): STOOL COPROCULTURE: Negative

SAE Supplemental Procedure	

NOT REPORTED

AE Stopped Rx Day	420
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ARTICULAR PAINS
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

フランス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，治験責任医師主導治験で盲検化された治験薬及びリサンキズマブが投与され，体軸性及び末梢性関節障害の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病（回腸結腸），回盲部腸切除，末梢性関節障害，片頭痛，体軸性関節障害（仙腸骨炎や強直性脊椎炎を含む），末梢性関節痛増加，非喫煙者及び非飲酒者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，レスキュー治療としてリサンキズマブの非盲検投与が開始された。

投与 416 日後，被験者は体軸性及び末梢性関節障害を発現した。投与 420 日後，体軸性及び末梢性関節障害は消失した。

投与 416 日後，被験者は入院した。徴候・症状は，呼吸困難感，耐え難い機械的疼痛，及び非常に重度の疲労を伴う，末梢性及び体軸性関節痛の突き上げ（膝，背部，手指，胸部）であった。投与 420 日後，被験者は退院した。

投与された薬剤は，Izalgi 及びアミトリプチリンであった。

The patient's past medications include:

SOLUPRED for CROHN'S DISEASE ([redacted])

HYDROCORTISONE for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Arthropathy (10003285) (Arthropathy (10003285)) [v.23.1] [10003285]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

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1) Arthropathy (10003285) (Arthropathy (10003285)) [v.23.1] [10003285]

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 AXIAL AND PERIPHERAL ARTHROPATHY

- Investigator: ARTICULAR PAINS

- AbbVie: Event is more likely related to pre-existing peripheral arthropathy (20[redacted]) and subject has been having ongoing axial arthropathy since [redacted] 20[redacted]. Additional risk factor includes pre-existing Crohn's disease.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of AXIAL AND PERIPHERAL ARTHROPATHY

- Investigator: ARTICULAR PAINS

- AbbVie: Event is more likely related to pre-existing peripheral arthropathy (20[redacted]) and subject has been having ongoing axial arthropathy since [redacted] 20[redacted]. Additional risk factor includes pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] 20[redacted] COPROCULTURE: Negative

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
背部痛	X			
心機能障害	X			
腱障害	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	6[redacted]	MALE	WHITE

Medical History	Onset Year
DIABETES MELLITUS	NOT REPORTED
HYPERTENSION	NOT REPORTED
LATENT TUBERCULOSIS	NOT REPORTED
OSTEOPOROSIS	NOT REPORTED
OTHER: CHRONIC OBSTRUCTIVE PULMONARY DISEASE	NOT REPORTED
OTHER: PULMONARY EMBOLISM	NOT REPORTED
OTHER: SPONDYLITIS	NOT REPORTED
SLEEP APNEA	NOT REPORTED
CROHN'S DISEASE	19[redacted]
MYOCARDIAL INFARCTION	20[redacted]
MYOCARDIAL INFARCTION	20[redacted]
OTHER: PERICARDITIS	20[redacted]
DEPRESSION: ANXIO-DEPRESSIVE SYNDROME	20[redacted]
OTHER: PNEUMOCYSTOSIS	20[redacted]
OTHER: ACUTE CORONARY SYNDROME	20[redacted]
OTHER: HYPERCHOLESTEROLEMIA	20[redacted]
OTHER: INTERCOSTAL ZONA	20[redacted]
OTHER: CHRONIC INTESTINAL ABSORPTION DISORDERS	20[redacted]
OTHER: INSOMNIA	20[redacted]
TUBERCULOSIS: LATENT TUBERCULOSIS	20[redacted]
OTHER: ARTHROPATHY	20[redacted]
OTHER: ASTHENIA	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	19[redacted]
CROHN'S DISEASE SURGICAL HISTORY: STRICTUREPLASTY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	3 CIGARETTE	45	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 29	[redacted] / 29	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 57	[redacted] / 57	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 92	[redacted] / 92	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 162	[redacted] / 162	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 212	[redacted] / 212	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 274	[redacted] / 274	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 316	[redacted] / 316	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 358	[redacted] / 358	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 423	[redacted] / 423	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	TID	Y-M: 20[redacted]
CLOPIDOGREL	75 mg	OTHER: DAILY	Y-M: 20[redacted]
APIXABAN	2.5 mg	OTHER: TWICE PER DAY	Y-M: 20[redacted]
CANDESARTAN	4 mg	OTHER: DAILY	Y-M: 20[redacted]
ESCITALOPRAM	10 mg	OTHER: DAILY	Y-M: 20[redacted]
PREGABALIN	50 mg	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]
AZATHIOPRINE	175 mg	QD	Y-M: 20[redacted]

ADALIMUMAB	40 mg	OTHER: EVERY 2 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: UNK	Y-M: 20[redacted]
METHOTREXATE	25 mg	OTHER: EVERY WEEK	Y-M: 20[redacted]
BACTRIM	800/160MG mg	OTHER: DAILY	Y-M: 20[redacted]
COLESTYRAMINE	4 g	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]
FOLIC ACID	5 mg	OTHER: DAILY	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: WEEK 0, WEEK 2, WEEK 6	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	OTHER: DAILY	Y-M: 20[redacted]
PARACETAMOL	1 g	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]
ACEBUTOLOL	200 mg	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]
LEKOVIT CA	500MG/400UI OTHER: MG/UI	OTHER: TWICE PER DAY	Y-M: 20[redacted]
ROSUVASTATIN	10 mg	OTHER: DAILY	Y-M: 20[redacted]
ZOPICLONE	7.5 mg	OTHER: DAILY	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
TRAMADOL	50 mg	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted]
USTEKINUMAB	390 mg	OTHER: ONCE	Y-M: 20[redacted]
USTEKINUMAB	90 mg	OTHER: EVERY MONTH)	Y-M: 20[redacted]
BUDESONIDE W/FORMOTEROL FUMARATE	200 ug	OTHER: 6 PER DAY	Y-M: 20[redacted] / -308
GAVISCON	10 mL	OTHER: THREE TIME PER DAY	Y-M: 20[redacted] / -254
SALBUTAMOL	100 ug	OTHER: TWICE PER DAY	Y-M: 20[redacted] / -254
TIOTROPIUM	2.5 ug	OTHER: 1 TO 6 PER DAY	Y-M: 20[redacted] / -254
RIFINAH	300 mg	QID	Y-M: 20[redacted] / -69

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
CLOPIDOGREL	75 mg	OTHER: DAILY	Y-M: 20[redacted]	ONGOING
APIXABAN	2.5 mg	OTHER: TWICE PER DAY	Y-M: 20[redacted]	ONGOING
CANDESARTAN	4 mg	OTHER: DAILY	Y-M: 20[redacted]	ONGOING
ESCITALOPRAM	10 mg	OTHER: DAILY	Y-M: 20[redacted]	ONGOING

PREGABALIN	50 mg	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]	ONGOING
BACTRIM	800/160MG mg	OTHER: DAILY	Y-M: 20[redacted]	ONGOING
COLESTYRAMINE	4 g	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]	ONGOING
FOLIC ACID	5 mg	OTHER: DAILY	Y-M: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg	OTHER: DAILY	Y-M: 20[redacted]	ONGOING
PARACETAMOL	1 g	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]	ONGOING
ACEBUTOLOL	200 mg	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]	ONGOING
LEKOVIT CA	500MG/400UI OTHER: MG/UI	OTHER: TWICE PER DAY	Y-M: 20[redacted]	ONGOING
ROSUVASTATIN	10 mg	OTHER: DAILY	Y-M: 20[redacted]	ONGOING
ZOPICLONE	7.5 mg	OTHER: DAILY	Y-M: 20[redacted]	ONGOING
TRAMADOL	50 mg	OTHER: THREE TIME PER DAY	Y-M: 20[redacted]	ONGOING
BUDESONIDE W/FORMOTEROL FUMARATE	200 ug	OTHER: 6 PER DAY	Y-M: 20[redacted] / -308	ONGOING
GAVISCON	10 mL	OTHER: THREE TIME PER DAY	Y-M: 20[redacted] / -254	ONGOING
SALBUTAMOL	100 ug	OTHER: TWICE PER DAY	Y-M: 20[redacted] / -254	ONGOING
TIOTROPIUM	2.5 ug	OTHER: 1 TO 6 PER DAY	Y-M: 20[redacted] / -254	ONGOING
DIPROSPAN	UNK OTHER: UNK	OTHER: ONCE	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 123
LIDOCAINE	UNK OTHER: UNK	OTHER: ONCE	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 123
VERAPAMIL	UNK OTHER: UNK	OTHER: UNK	Y-M: 20[redacted] / 271	Y-M: 20[redacted] / 362
MACROGOL	10 g	TID	Y-M: 20[redacted] / 353	Y-M: 20[redacted] / 353
MORPHINE	10 mg	OTHER: UNK	Y-M: 20[redacted] / 353	Y-M: 20[redacted] / 353
MORPHINE	5 mg	OTHER: UNK	Y-M: 20[redacted] / 353	Y-M: 20[redacted] / 353

Event #1: Serious Adverse Event

Event Description	TENDINOPATHY
Preferred Term	腱障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 123
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 123): INJECTION OF A DIPROSTENE BULB IN EACH SUB-ACROMIO-DELTOID PURSE:FAVORABLE ISSUE; PERFORMED BILATERAL SUBACROMIO-DELTOID BURSA INFILTRATIONS:THE GESTURE WAS MADE ON [redacted]/[redacted]/20[redacted] WITH INJECTION OF A DIPROSSTEN BULB IN EACH SUB-ACROMIO-DELTOID BOURSE WITHOUT COMPLICATIONS DURING AND AT THE DECODERS. THE PATIENT REPORTS AN IMPROVEMENT IN PAIN

AE Stopped Rx Day	127
Duration of AE	5 DAYS
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DIABETES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	SUBACUTE LOW BACK PAIN
Preferred Term	背部痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 353
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 353): ELECTROCARDIOGRAM:REGULAR NON SINUSAL RHYTHM AT 64BPM WITH JUNCTIONAL EXHAUST AND P-WAVES RETROGRADES EVOKING SINUS DYSFUNCTION

AE Stopped Rx Day	354
Duration of AE	2 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SPONDYLOARTHITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	CARDIAC SINUS DYSFUNCTION
Preferred Term	心機能障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 354
Age at AE Onset	6[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 354): NPTST534-TROPONINE: 5 [NOT REPORTED - 53] NG/L
Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 354): ELECTROCARDIOGRAM:REGULAR NON SINUSAL RHYTHM AT 64BPM WITH JUNCTIONAL EXHAUST AND RETROGRADE P-WAVES EVOKING ASINUS DYSFUNCTION

AE Stopped Rx Day	355
Duration of AE	2 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	THE SEQUELS WERE SIMPLE. AFTER THE ISOPTINE SHUTDOWN EVERYTHING IS BACK TO NORMAL.
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

フランス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，腱障害の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，関節障害，2 ヵ所の肩峰下三角筋滑液包浸潤，脊椎炎，糖尿病，喫煙者（1 日 3 本を 45 年間）及び元飲酒者（1 日 2 杯未満）であった。

投与 123 日後，被験者は腱障害を発現した。投与 127 日後，腱障害は消失した。

投与 122 日後，被験者は肩痛のため入院した。両側の肩峰下三角筋滑液包浸潤が認められ，それぞれの肩峰下三角筋滑液包に Diprostene 1 アンプルの注射が行われた。入院中，合併症は認められなかった。被験者は，注射後疼痛の改善を報告した。投与 127 日後，被験者は退院した。

The patient's past medications include:

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

RIFINAH for TB PROPHYLAXIS ([redacted]20[redacted] - [redacted]20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Tendinopathy (10080130) (Tendon disorder (10043239)) [v.23.1] [10080130]

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 TENDINOPATHY

- Investigator: Diabetes

- AbbVie: Risk factors include pre-existing spondylitis, arthropathy and smoking

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

フランス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，亜急性腰痛及び洞機能不全の事象を発現した。

Event 2 及び 3 の臨床経過：

関連する病歴は，クローン病，心筋梗塞，急性冠動脈症候群，高コレステロール血症，狭窄形成，関節障害，慢性閉塞性肺疾患，脊椎炎，糖尿病，高血圧，喫煙者（1 日 3 本を 45 年間），元飲酒者（1 日 2 杯未満）及び肺塞栓症であった。

投与 353 日後，被験者は亜急性腰痛を発現した。投与 354 日後，被験者は洞機能不全を発現した。投与 354 日後，亜急性腰痛は消失した。投与 355 日後，洞機能不全は消失した。

投与 353 日後，被験者は，クローン病に関連している脊椎炎の一部としての下背部痛の診断目的及び鎮痛剤の調整目的のリウマチ学的検査のため，入院した。モルヒネによる治療が開始された。徴候・症状は，最近数週間の激しい背部痛，腰椎低下，歩行距離の限度（60 m），また前屈の増加もあった。投与 354 日後，被験者は退院し，杖をついて歩けるようになった。

投与 354 日後，被験者は，Isoptine の最終変更後に数回厄介な動悸が発症したため，再入院した。ECG が行われた結果，64 bpm の一定の非洞調律が認められ，洞機能不全を誘発している接合部消耗及び逆行性 P 波を伴っていた。心臓病学的な意見が必要となり，被験者はトロポニン／BNP を陰性に戻す用量を得ることができた。結果は単純であった。Isoptine 投与停止後，すべて正常に戻った。投与 355 日後，被験者は退院した。

投与された薬剤は，Actiskenan 及び Skenan であった。

The patient's past medications include:

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

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

INFLECTRA 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])

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

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

RIFINAH for TB PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Low back pain (10024891) (Back pain (10003988)) [v.23.1] [10024891]

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

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

Dechallenge: Not Applicable

2) Cardiac dysfunction (10079751) (Cardiac dysfunction (10079751)) [v.23.1] [10079751]

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 SUBACUTE LOW BACK PAIN

- Investigator: Spondyloarthitis

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

Event of CARDIAC SINUS DISFUNCTION

- Investigator: The sequels were simple. After the Isoptine shutdown everything is back to normal.

- AbbVie: Risk factors include concomitant use of Isoptine, prior myocardial infarctions and pre-existing acute coronary syndrome.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ELECTROCARDIOGRAM:** Regular non sinusal rhythm at 64 bpm with junctional exhaust and retrograde P-waves evoking a sinus dysfunction.

[redacted] **ELECTROCARDIOGRAM:** Regular non sinusal rhythm at 64 bpm with junctional exhaust and retrograde P-waves evoking a sinus dysfunction.

[redacted] **TROPONINE:** 5 NG/L (normal <53)

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			
憩室炎	X	X		X
肛門周囲痛	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
MIGRAINE HEADACHE: TENSIONAL HEADACHE	NOT REPORTED
OTHER: ARTHRALGIAS	NOT REPORTED
OTHER: IRRITABLE COUGH	NOT REPORTED
OTHER: OBESITY	NOT REPORTED
INFLAMMATORY BOWEL DISEASE: ABDOMINAL PAIN	20[redacted]
CROHN'S DISEASE	20[redacted]

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	FORMER		15	20[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)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 20	[redacted]20[redacted] / 20	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 48	[redacted]20[redacted] / 48	1

PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 85 85	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 141 141	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 197 197	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 268 268	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 309 309	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 357 357	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]
NOLOTIL	575 mg	PRN	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
PARACETAMOL	1 g	PRN	NOT REPORTED	ONGOING
ULTRACET	ND OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 141	ONGOING
DIAZEPAM	5 mg	QD	Y-M: 20[redacted] / 317	ONGOING
METAMIZOLE	0.8 g	PRN	Y-M: 20[redacted] / 317	ONGOING
ULTRACET	37.5/325 mg	PRN	Y-M: 20[redacted] / 317	ONGOING
METAMIZOLE	2 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 326	Y-M: 20[redacted] / 327
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 326	Y-M: 20[redacted] / 327
PARACETAMOL	1 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 326	Y-M: 20[redacted] / 327
LOCAL ANESTHETICS	UNK g	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 338
GLYCERYL TRINITRATE	UNK g	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 341
PLANTAGO OVATA	3.5 mg	BID	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 341
GLYCERYL TRINITRATE	UNK g	OTHER: EVERY 12 HOURS	Y-M: 20[redacted] / 341	ONGOING

LOCAL ANESTHETICS	UNK g	PRN	Y-M: 20[redacted]- / 341	ONGOING
PARAFFIN	7.173,9 mg	QD	Y-M: 20[redacted]- / 341	ONGOING
PLANTAGO OVATA	7 g	QD	Y-M: 20[redacted]- / 341	ONGOING
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted]- / 401	Y-M: 20[redacted]- / 409

Event #1: Serious Adverse Event

Event Description	WORSENING CROHN'S DISEASE
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 326
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 326): NPTST090-C-REACTIVE PROTEIN: 59.6 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 326): FISTULA SURGERY, DRAINED THE FISTULA:IMPROVED THE HEALTH OF PATIENT AND SHE IS DISCHARGE

AE Stopped Rx Day	327
Duration of AE	2 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

Event #2: Serious Adverse Event

Event Description	POST-DEFECATORY PROCTALGIA
Preferred Term	肛門周囲痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 337
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 341): MRI:LINEAR INTERSPHERICAL FISTULA AT 5H-6H WITH NO EVIDENCE OF ABSCESSED COLLECTIONS OR INVOLVEMENT OF ISCHIOANAL FAT (GRADE I) PARIETAL THICKENING AND MULTIPLE SIGMA DIVERSIONS NO SIGNIFICANT INGUINAL

AE Stopped Rx Day	341
Duration of AE	5 DAYS

Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	WORSENING THE OTHER AE, PAIN IN THE ANAL AREA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	DIVERTICULITIS
Preferred Term	憩室炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 399 (42 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 399): C Reactive Protein: 128.9 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (Rx Day 400): STOOL COPROCULTURE: Negative; STOOL SHIGA E.COLI TOXIN: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 399): THORACIC X-RAY:NORMAL; [redacted]20[redacted] (Rx Day 400): COMPUTERIZED AXIAL TOMOGRAPHY:ABDOMINAL SIGMA-WALL FISTULA AND SMALL INTRA-ABDOMINAL ABSCESS IN PELVIS BEST SECONDARY TO COMPLICATED DIVERTICULITIS OR TRANSMURAL COMPLICATION IN PATIENT WITH CROHN'S DISEASE

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	WORSENING OF DIVERTICULITIS
Preferred Term	憩室炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 421 (64 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 422): CT SCAN:ANFRACTUOUS COLLECTION WITH 5 CM WATER LEVEL IN RETZIUS SPACE SECONDARY TO FISTULIZATION OF ORIGENSIGMOID.

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING

Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	FISTUALIZATION OF THE SIGMOID ORIGIN IS THE CAUSE OF THE WORSENING OF DIVERTICULITIS
Discontinued Study Drug Due to the Event	YES
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

スペイン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，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，元喫煙者（15 年間），炎症性腸疾患（腹痛），クローン病，肥満及び非飲酒者であった。

投与 326 日後，被験者はクローン病悪化を発現した。投与 327 日後，クローン病悪化は消失した。

本事象発現前の投与 317 日後，被験者は肛門痛（非重篤）を発現した。

投与 326 日後，被験者は肛門痛及び不快感のため入院した。排膿を伴う外瘻孔が認められた。同日，被験者は手術及び外瘻孔のドレナージを受けた。投与 327 日後，被験者の健康状態は改善され，被験者は退院した。

投与された薬剤は，パントプラゾール，メトロニダゾール，paracetamol 及び Metamizol であった。

The patient's past medications include:

CIPROFLOXACINO for ANAL PAIN ([redacted] 20[redacted] - [redacted] 20[redacted])

METRONIDAZOL for ANAL PAIN ([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 CROHN'S DISEASE

- Investigator: Crohn's disease.

- AbbVie: Event is most like related to pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BODY WEIGHT: 10[redacted] KG

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 59.6 MG/L (normal 0.0 to 5.0)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

スペイン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，排便後肛門周囲痛の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，元喫煙者（15 年間），炎症性腸疾患及びクローン病であった。

投与 337 日後，被験者は排便後肛門周囲痛を発現した。投与 341 日後，排便後肛門周囲痛は消失した。

本事象発現前の投与 317 日後，被験者は肛門痛（非重篤）を発現した。

投与 327 日後，被験者は痔瘻に対する矯正手術を受けた。術後，疼痛は改善しなかった。投与 337 日後，被験者は肛門痛の悪化及び便秘のため再入院した。投与 341 日後，被験者は退院した。

投与された薬剤は，Titanoreine，Plantaben，Emuliquen simple［パラフィン］及び Rectogesic であった。

The patient's past medications include:

CIPROFLOXACINO for ANAL PAIN ([redacted])

METRONIDAZOL for ANAL FISTULA and ANAL PAIN ([redacted])

METAMIZOL for ANAL FISTULA ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Proctalgia (10036772) (Proctalgia (10036772)) [v.23.0] [10036772]

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 POST-DEFECATORY PROCTALGIA

- Investigator: worsening the other ae, pain in the anal area

- AbbVie: Event is more likely related to complications associated with crohn's disease with presence of anal fistula.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL MRI:** LINEAR INTERSPHERICAL FISTULA AT 5H-6H WITH NO EVIDENCE OF ABSCESSED COLLECTIONS OR INVOLVEMENT OF ISCHIOANAL FAT (GRADE I). PARIETAL THICKENING AND MULTIPLE SIGMA DIVERSIONS .NO SIGNIFICANT INGUINAL OR LOCOREGIONAL ADENOPATHIES ARE OBSERVED. NO EVIDENCE OF FREE LIQUID AT THE BOTTOM OF THE BAG. BLADDER AND RECTUM WITHOUT FINDINGS OF SIGNIFICANCE

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

スペイン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，憩室炎及び憩室炎悪化の事象を発現した。

Event 3及び4の臨床経過：

関連する病歴は，元喫煙者（15年間），腹痛，クローン病（回腸，非狭窄型，非穿通型），肥満及び非飲酒者であった。

投与399日後，被験者は憩室炎を発現した。投与421日後，被験者は憩室炎悪化を発現した。

投与399日後，被験者は急性憩室炎のため入院した。徴候・症状は発熱，下痢及び腹痛であった。身体的診察の結果，触診時，特に左腸骨窩に腹痛が認められた。その他の関連する症状や徴候は認められなかった。胸部X線検査の結果は正常であった。CTスキャン検査の結果，クローン病の被験者の合併症の憩室炎に続発した腹部S状結腸壁瘻孔が認められた。投与401日後，被験者は退院した。

投与415日後，被験者は腹部膿瘍（非重篤）を発現した。

投与421日後，被験者は腹痛及び発熱のため入院した。抗生剤に対して反応がなく，憩室炎悪化と診断された。投与430日後，被験者は退院した。

憩室炎悪化の事象により治験薬の投与が中止され，被験者は治験参加を中止した。

投与された薬剤は，Cefixima，メトロニダゾール及びシプロフロキサシンであった。

Causality for RISANKIZUMAB (Blinded)

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1) Diverticulitis (10013538) (Diverticulitis (10013538)) [v.23.0] [10013538]

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

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

Dechallenge: Not Applicable

2) Diverticulitis aggravated (10048388) (Diverticulitis (10013538)) [v.23.0] [10048388]

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 DIVERTICULITIS

- Investigator: Crohn Disease.

- AbbVie: Risk factors include age, high BMI and pre-existing Crohn's disease.

Event of WORSENING OF DIVERTICULITIS

- Investigator: Fistualization of the sigmoid origin is the cause of the worsening of diverticulitis.

- AbbVie: Risk factors include age, high BMI and pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BMI: 41.6 kg/m2

[redacted] **20[redacted] COMPUTERIZED AXIAL TOMOGRAPHY:** Abdominal sigma-wall fistula and small intra-abdominal abscess in pelvis best secondary to complicated diverticulitis or transmural complication in patient

with Crohns disease

[redacted] 20[redacted] COPROCULTURE: Negative

[redacted] **20[redacted] CT:** ANFRACTUOUS COLLECTION WITH 5 CM WATER LEVEL IN RETZIUS SPACE SECONDARY TO FISTULIZATION OF ORIGENSIGMOID.

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 128.9 MG/L (normal 0.0 to 5.0)

[redacted] 20[redacted] SHIGA E.COLI TOXIN: Negative

[redacted] 20[redacted] THORACIC X-RAY: 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
結腸異形成	X	X		

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: ANEMIA	20[redacted]
OTHER: CHRONIC GASTRITIS	20
CROHN'S DISEASE	20
OTHER: ANKYLOSING SPONDILITIS	20
OTHER: PSORIASIS OF THE SCALP	20
INFLAMMATORY BOWEL DISEASE: DRAINING ABDOMINAL FISTULAS	20
OTHER: VITAMIN D3 DEFICIT	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)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 58	[redacted]20[redacted] / 58	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 86	[redacted]20[redacted] / 86	1

PLACEBO	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 143 143	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 204 204	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 253 253	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 316 316	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 373 373	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 432 432	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: 19[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
COLECALCIFEROL	1000 IU	QD	Y-M: 20[redacted] / 86	ONGOING

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

Event Description HIGH GRADE DYSPLASIA ON THE TRANSVERSE COLON (AT THE SURGICAL ANASTOMOSIS)

Preferred Term 結腸異形成

AE Onset Date / Rx Day 20[redacted] / 451 (19 DAYS AFTER LAST TREATMENT)

Age at AE Onset 2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

20[redacted] (Rx Day 451): OTHER COLONOSCOPY BIOPSY HISTOPATHOLOGICAL EXAMINATION: Positive-HIGH GRADE DYSPLASIA IDENTIFIED ON ONE OF THE BIOPSY SAMPLES; 20[redacted] (Rx Day 487): OTHER RESECTION SPECIMEN FROM RIGHT COLECTOMY HISTOPATHOLOGICA EXAMINATION: Negative-CHRONIC GRANULOMATOUS INFLAMATION WITH HIGH ACTIVITY

SAE Supplemental Procedure

20[redacted] (Rx Day 451): COLONOSCOPY:AT THE LEVEL OF COLO-COLIC ANASTOMOSIS: ACTIVE LESIONS WITH ERYTHEMATOUS MUCOSA AND MULTIPLE POLYPS_INVOLVING CIRCUMFERENTIALLY THE ANASTOMOSIS (BIOPSIES OBTAINED); 20[redacted] (Rx Day 487): RIGHT COLECTOMY WITH ILEO-COLIC ANASTOMOSIS:FAVORABLE OUTCOME

AE Stopped Rx Day 495 (63 DAYS AFTER LAST TREATMENT)

Duration of AE 45 DAYS

Severity MODERATE

Relation to Study Drug by Investigator No Reasonable Possibility

Investigator Alternative Etiology	CROHN'S DISEASE EVOLUTION
Discontinued Study Drug Due to the Event	YES
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

ルーマニア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，横行結腸（外科的吻合部）の高度異形成の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，貧血，慢性胃炎，クローン病（L2：結腸疾患），強直性脊椎炎，排膿を伴う腹部瘻孔，ビタミン D3 欠乏，非喫煙者及び禁酒であった。

被験者は，先行試験 M15-991 に組み入れられ（被験者番：[redacted]），20[redacted]年[redacted]月[redacted]日から20[redacted]年[redacted]月[redacted]日まで，盲検化された治験薬の投与を受けた。

投与 451 日後，被験者は，横行結腸（外科的吻合部）の高度異形成を発現した。投与 495 日後，横行結腸（外科的吻合部）の高度異形成は消失した。

以前，Week 52（投与 451 日後）時の結腸内視鏡検査の結果，被験者は高度異形成と診断され，外科的評価が予定された。

投与 487 日後，被験者は手術の目的で入院した。治験責任医師によると，被験者には重要な徴候・症状はなく，クローン病は臨床的寛解状態であった。同日，被験者は回腸結腸吻合を伴う右半結腸切除を受け，術後の経過は良好であった。投与 495 日後，被験者は退院した。

治験責任医師によると，被験者には本事象に関連する家族歴はなかった。

Causality for RISANKIZUMAB (Blinded)

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1) Colon dysplasia (10071161) (Colon dysplasia (10071161)) [v.23.1] [10071161]

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 HIGH GRADE DYSPLASIA ON THE TRANSVERSE COLON (AT THE SURGICAL ANASTOMOSIS

- Investigator: Crohn's disease evolution.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] COLON BIOPSY:** HIGH GRADE DYSPLASIA IDENTIFIED ON ONE OF THE BIOPSY SAMPLES

[redacted] **20[redacted] COLONOSCOPY:** At the level of colo-colic anastomosis: active lesions with erythematous mucosa and multiple polyps involving circumferentially the anastomosis (biopsies obtained)

[redacted] 20[redacted] HISTOPATHOLOGICAL EXAMINATION: Positive

[redacted] **20[redacted] HISTOPATHOLOGICAL EXAMINATION:** CHRONIC GRANULOMATOUS INFLAMATION WITH HIGH ACTIVITY

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
靭帯断裂	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: ALC TEAR LEFT KNEE	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: STOMACHACHE	20[redacted]

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)
M15991 /UNKNOWN		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 84	[redacted]20[redacted] / 84	1

RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 140	20[redacted] / 140	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 196	20[redacted] / 196	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 256	20[redacted] / 256	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 311	20[redacted] / 311	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 365	20[redacted] / 365	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 417	20[redacted] / 417	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
SANALEPSI	10 mg	PRN	Y-M: 20[redacted]
ZOPICLONE	7.5 mg	PRN	Y-M: 20[redacted]
INFLIXIMAB	5 MG/KG W 0, 2, 6 mg/kg	EVERY 2 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	Q2M	Y-M: 20[redacted]
METAMIZOLE	500 mg	PRN	Y-M: 20[redacted]
TRAMADOL	100 mg	PRN	Y-M: 20[redacted]
INFLIXIMAB	10 mg/kg	QM	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	Q2M	Y-M: 20[redacted]
ADALIMUMAB	160 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	80 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: ONCE ONLY	Y-M: 20[redacted]
CERTOLIZUMAB	400 mg	QM	Y-M: 20[redacted] / -214
D-CALSOR	UNKNOWN mg	QD	Y-M: 20[redacted] / -209
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -53
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / -30
AIDA	0.02/3 mg	QD	Y-M: 20[redacted] / 35

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
OPTIDERM	30/50 mg	PRN	Y-M: 20[redacted] / 187	NOT REPORTED
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted] / 196	NOT REPORTED
BETADERMIC	UNKNOWN OTHER: UNKNOWN	OTHER: 1X 2 WOCHE	Y-M: 20[redacted] / 297	NOT REPORTED
BILASTINE	20 mg	QD	Y-M: 20[redacted] / 297	NOT REPORTED

METHYLPREDNISOLONE	UNKNOWN OTHER: UNKNOWN	OTHER: 1X 2 WOCHE	Y-M: 20[redacted] / 297	NOT REPORTED
MOMETASONE	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / 297	NOT REPORTED
ZOPICLONE	7.5 mg	QD	Y-M: 20[redacted] / 312	NOT REPORTED

Event #1: Serious Adverse Event

Event Description	WORSENING ACL TEAR LEFT KNEE
Preferred Term	靭帯断裂
AE Onset Date / Rx Day	[redacted]20[redacted] / 379
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	381
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ACL TEAR
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

スイス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，左膝前十字靭帯断裂の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，前十字靭帯断裂，左膝前十字靭帯断裂，非喫煙者及び非飲酒者であった。

投与 379 日後，被験者は左膝前十字靭帯断裂の悪化を発現した。投与 381 日後，左膝前十字靭帯断裂の悪化は消失した。

投与 379 日後，被験者は左膝痛のため入院し，左膝前十字靭帯断裂（初回診断は投与の約 5 年前）の悪化と診断された。被験者は左十字靭帯修復といわれている前十字靭帯再建術を受けた。投与 381 日後，被験者は退院した。

The patient's past medications include:

INFLIXIMAB for CROHN'S DISEASE ([redacted])

VEDOLIZUMAB for CROHN'S DISEASE ([redacted])

ADALIMUMAB for CROHN'S DISEASE ([redacted])

CERTOLIZUMAB for CROHN'S DISEASE ([redacted])

PREDNISON for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Anterior cruciate ligament tear (10059062) (Ligament rupture (10065433)) [v.22.1] [10059062]

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 ACL TEAR LEFT KNEE

- Investigator: ACL Tear.

- AbbVie: event is most likely related to pre-existing history of ACL tear in left knee. Additional risk factor includes female gender.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BODY WEIGHT: 6[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	X		

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
DEPRESSION: PACIENT HAS DEPRESSION AND ANXIETY	20[redacted]
OTHER: GONARTROSIS	20[redacted]
OTHER: PACIENT HAD REACTION AFTER USES HUMIRA - FOLICULITIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: VOMITTING	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	10 CIGARETTE	15	
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)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 36	[redacted]20[redacted] / 36	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
VENLAFAXINE	150 mg	BID	Y-M: 20[redacted]
BELOSALIC	0,5MG+20MG UNG g	QD	Y-M: 20[redacted] / -201

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
NADROPARIN	0,4 mL	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 169
NADROPARIN	0.4 mL	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 169
FORTRANS	2 OTHER: SACHET	QD	Y-M: 20[redacted] / 183	Y-M: 20[redacted] / 184
POTASSIUM	1000 mg	OTHER: [redacted], TWICE A DAY, [redacted] ONCE A DAY	Y-M: 20[redacted] / 183	Y-M: 20[redacted] / 184
POTASSIUM	1000 mg	QD	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 185
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 186	Y-M: 20[redacted] / 191
METAMIZOLE	500 mg	OTHER: TID FROM [redacted] TO [redacted] 20[redacted].BID ON [redacted]	Y-M: 20[redacted] / 186	Y-M: 20[redacted] / 191
ALUMINIUM ACETATE	UNKNOWN	PRN	Y-M: 20[redacted] / 186	Y-M: 20[redacted] / 527
ULTRACET	37.5 + 325 mg	OTHER: FROM [redacted] TO [redacted] TID, [redacted] BID	Y-M: 20[redacted] / 187	Y-M: 20[redacted] / 191
NUTRIENTS NOS	500 mL	OTHER: 20 ML/ HOUR [redacted] TO [redacted], 60 ML/ HOURS ON [redacted]	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 220

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

Event Description	WORSENING OF CROHN DISEASE
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 167 (82 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 167): Erythrocytes: 4.8 [3.8 - 5.2] 10^12/L; NPTST160-CRP: 85.4 [0 - 10] MG/L;
[redacted]20[redacted] (Rx Day 168): NPTST083-C - REACTIVE PROTEIN: 71.7 [0 - 10] MG/L
Microbiology
[redacted]20[redacted] (Rx Day 167): STOOL E .COLLI, KLEBSIELLA: Negative
SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 167): ECG:NORMAL; ULTRASOUND:SIGNS OF COLON INFLAMATION;
[redacted]20[redacted] (Rx Day 168): X RAY- RIGHT KNEE:NORMAL

AE Stopped Rx Day	170 (85 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PROGRESSION OF UNDERLYING DISEASE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	RELAPSE OF CROHN DISEASE
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 183 (98 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 183): Leukocytes: 19.8 [4 - 10] 10^9/L; Potassium: 3.8 [3.8 - 5.2] MMOL/L; [redacted]20[redacted] (Rx Day 188): C Reactive Protein: 152 [0 - 10] MG/L
Microbiology
[redacted]20[redacted] (Rx Day 186): OTHER EVACUATION 50 ML NON INFLAMATORY LIQUID PUNCTION / EVACUATION: -LIQUID NOT MICROBIOLOGICALLY EXAMINATED
SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 183): ECG:NORMAL; [redacted]20[redacted] (Rx Day 184): ILEOCOLONOSCOPY:RELAPSE OF CROHN DISEASE; [redacted]20[redacted] (Rx Day 186): SONOGRAPHY OF THE RIGHT KNEE:BURSITIS SUPRAPATELARIS - RIGHT KNEE, EVACUATION OF 50 ML NON INFLAMATORY LIQUID; [redacted]20[redacted] (Rx Day 189): NASAL-JEJUNAL TUBE INSERTED:THE TUBE PLACED - DUE TO RELAPS OF CD AND EXHAUSTAION OF ALL TREATMENT POSSIBILITIES OF CD; [redacted]20[redacted] (Rx Day 314): AXIAL ILEOSTOMY AND REVISION OF PERINEUM:NO IMPROVEMENT; [redacted]20[redacted] (Rx Day 428): RE-DRAINAGE OF PERINEUM:NO BIOPSY DONE, OPERATION AND AFTER OPERATION THE PATIENT WAS WITHOUT ANY CONPLICATIONS AND DISCHARGED IN STABLE CONDITION

AE Stopped Rx Day	191 (106 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PROGRESION OF CROHN DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

チェコ共和国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，クローン病悪化及びクローン病再燃の事象を発現した。

Event 1及び2の臨床経過：

関連する病歴は，腸切除，変形性膝関節症，クローン病，嘔吐，喫煙者（1日10本を15年間）及び非飲酒者であった。

投与167日後，被験者はクローン病悪化を発現した。投与170日後，クローン病悪化は消失した。投与183日後，被験者はクローン病再燃を発現した。投与191日後，クローン病再燃は消失した。

投与167日後，被験者はクローン病悪化のため入院した。CRP増加，及び全身健康状態の悪化が認められた。コルチコイド及び抗生剤を含む治療が行われた。症状は改善した。投与170日後，被験者は退院した。被験者は規定来院を継続していなかったため，2ヵ月半以上治験薬の投与を受けていなかった。治験薬の投与が完全に中止された。

投与183日後，被験者は計画されていた結腸内視鏡検査のため入院した。投与184日後，回腸結腸内視鏡検査が行われ，クローン病再燃（結腸の重度の炎症）が認められた。クローン病再燃及びクローン病に対するすべての治療の可能性を使い尽くしてしまったため，経鼻空腸チューブが挿入され，抗生剤も開始された。手術が適応となった。投与186日後，被験者は右膝超音波検査を受け，その結果，膝蓋上包滑液包炎が認められ，非炎症性液体50 mLが排出された。その液体の生物学的検査は行われなかった。投与191日後，被験者は安定した状態で退院し，手術のために待機していた。

投与から約8ヵ月後，被験者は本治験への参加の同意を撤回した。

投与から約11ヵ月後，改善しないため，被験者は体軸方向の回腸瘻造設及び会陰部修正を受けた。投与428日後，会陰部の再ドレナージが行われ，生検は行われなかった。手術後，被験者

に合併症は認められなかった。

投与された薬剤は，Doxybene，メドロール，ソル・メドロール，Zaldiar，Klacid，Normix，Novalgin，Peptamen，Sefotak 及びメトロニダゾールであった。

Causality for RISANKIZUMAB (Blinded)

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1) Crohns disease aggravated (10011408) (Crohn's disease (10011401)) [v.23.1] [10011408]

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 relapse (10076318) (Crohn's disease (10011401)) [v.23.1] [10076318]

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 DISEASE

- Investigator: Progression of underlying disease

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

Event of RELAPSE OF CROHN'S DISEASE

- Investigator: Progression of Crohn disease

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 85.4 mg/dL (normal 0 to 10)

[redacted] **20[redacted] CRP:** 71.7 mg/dL (normal 0.0 to 10)

[redacted] **20[redacted] CRP:** 152 MG/L (normal 0 to 10)

[redacted] 20[redacted] ECG: normal

[redacted] 20[redacted] ECG: normal

[redacted] **20[redacted] ILEOCOLONOSCOPY:** revealed a relapse of Crohn’s disease (severe inflammation of the colon).

[redacted] **20[redacted] POTASSIUM:** 3.78 MMOL/L (normal 3.8 to 5.2)

[redacted] **20[redacted] RBC:** 4.78 X10**12/L ormal 3.80 to 5.20)

[redacted] **20[redacted] SONOGRAPHY:** bursitis suprapatellaris of the right knee. Evacuation of 50 ml non-inflammatory liquid and the liquid not microbiologically examined.

[redacted] **20[redacted] STOOL CULTURE:** E. Coli and Klebsiella: Negative

[redacted] **20[redacted] ULTRASOUND:** SIGNS OF COLON INFLAMATION

[redacted] **20[redacted] WBC:** 19.8 X10**9/L (normal 4 to 10)

[redacted] 20[redacted] X RAY RIGHT KNEE: 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
子宮内膜症	X			
亜イレウス	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: CD	NOT REPORTED
CROHN'S DISEASE	20[redacted]

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)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /UNKNOWN		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1

M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 93	[redacted]20[redacted] / 93	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 93	[redacted]20[redacted] / 93	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 149	[redacted]20[redacted] / 149	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 149	[redacted]20[redacted] / 149	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 204	[redacted]20[redacted] / 204	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 204	[redacted]20[redacted] / 204	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 261	[redacted]20[redacted] / 261	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 261	[redacted]20[redacted] / 261	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 317	[redacted]20[redacted] / 317	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 317	[redacted]20[redacted] / 317	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 370	[redacted]20[redacted] / 370	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 370	[redacted]20[redacted] / 370	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -21

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
NUTRIENTS NOS	1-2 OTHER: BOTTLE	PRN	Y-M: 20[redacted] / 98	ONGOING
DICLOFENAC	20 gtt	TID	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 165
PLASMA LYTE 148	1000 mL	OTHER: 100 ML/ HOUR	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 171
NADROPARIN	0.4 mL	QD	Y-M: 20[redacted] / 168	Y-M: 20[redacted] / 173
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 170	Y-M: 20[redacted] / 173

PLASMA LYTE 148	500 mL	OTHER: 100 ML/ PER HOUR	Y-M: 20[redacted] / 172	Y-M: 20[redacted] / 173
METAMIZOLE	500 mg	PRN	Y-M: 20[redacted] / 299	Y-M: 20[redacted] / 301
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 299	Y-M: 20[redacted] / 301
MOVIPREP	2000 mL	OTHER: SACHET	Y-M: 20[redacted] / 307	Y-M: 20[redacted] / 308
METAMIZOLE	500 mg	QD	Y-M: 20[redacted] / 328	Y-M: 20[redacted] / 328
OMEPRAZOLE	40 mg	PRN	Y-M: 20[redacted] / 328	Y-M: 20[redacted] / 328
PLASMA LYTE 148	500 mL	OTHER: 150 ML PER HOUR	Y-M: 20[redacted] / 328	Y-M: 20[redacted] / 329
PLASMA LYTE 148	500 mL	OTHER: 100 PER HOUR	Y-M: 20[redacted] / 329	Y-M: 20[redacted] / 329
PLASMA LYTE 148	1000 mL	OTHER: 100 ML PER HOUR	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 331
OLIMEL N5E	1000 mL	OTHER: 50 ML PER HOUR	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 335
NADROPARIN	0.3 mL	QD	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 341
PLASMA LYTE 148	1000 mL	OTHER: 50 ML PER HOUR	Y-M: 20[redacted] / 331	Y-M: 20[redacted] / 335
PLASMA LYTE 148	1000 mL	OTHER: 60 ML PER HOUR	Y-M: 20[redacted] / 335	Y-M: 20[redacted] / 336
PLASMA LYTE 148	1000 mL	OTHER: 80 ML PER HOUR	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 337
SUFENTANIL	250UG/25 ML ug	OTHER: 1- 2 ML PER HOUR	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 337
OLIMEL N5E	1000 mL	OTHER: 40 ML PER HOUR	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 339
AMBROXOL	5 mL	OTHER: [redacted]20[redacted] - [redacted]20[redacted] QID, [redacted]20[redacted] 3DOSES PER SIX HOURS, [redacted]20[redacted] ONE DOSE	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 340
METAMIZOLE	1000 mg	OTHER: [redacted]20[redacted] AND [redacted]20[redacted] 2 DOSES PER SIX HOURS, [redacted]20[redacted] - [redacted]20[redacted] QID	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 340
MORPHINE	20 mg	OTHER: 0.4-0.8 ML PER HOUR	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 338

PLASMA LYTE 148	1000 mL	OTHER: 30 ML PER HOUR	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 340
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 341	Y-M: 20[redacted] / 341

Event #1: Serious Adverse Event

Event Description	SUBILEUS
Preferred Term	亜イレウス
AE Onset Date / Rx Day	[redacted]20[redacted] / 166
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 167): Ketones: 3 [0 - 0] ARB.J.; [redacted]20[redacted] (Rx Day 170): Bilirubin: 7 [4 - 21] UMOL/L; C Reactive Protein: 74.6 [0 - 10] MG/L; [redacted]20[redacted] (Rx Day 171): C Reactive Protein: 39.8 [0 - 10] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 167): ABDOMEN XRAY:SUSPECTION ON SUBILEUS CONDITION; CHEST XRAY:NORMAL; ECG:NORMAL; [redacted]20[redacted] (Rx Day 169): ABDOMINAL ULTRASOUND:DILATATION OF LONG PART OF ILEUM

AE Stopped Rx Day	297
Duration of AE	132 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DIET MISTAKE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	WORSENED SUBILEUS
Preferred Term	亜イレウス
AE Onset Date / Rx Day	[redacted]20[redacted] / 298
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 299): C Reactive Protein: 4.4 [0 - 10] MG/L; Hemoglobin: 136 [120 - 160] G/L; Leukocytes: 12.4 [4 - 10] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 299): ABDOMINAL X - RAY:SUBILEUS OF SMALL INTESTINAL LOOPS; ECG:NORMAL

AE Stopped Rx Day	301
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility

Investigator Alternative Etiology	UNDERLYING DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	WORSENED SUBILEUS
Preferred Term	亜イレウス
AE Onset Date / Rx Day	[redacted]20[redacted] / 328
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 328): Hematocrit: 0.46 [0.35 - 0.47] FRACTION OF 1; Leukocytes: 33.7 [4 - 10] 10^9/L; 20[redacted] (Rx Day 329): Albumin: 37 [38 - 58] G/L; C Reactive Protein: 42.5 [0 - 10] MG/L; Hemoglobin: 117 [120 - 160] G/L; Potassium: 4.4 [3.8 - 5.2] MMOL/L

Microbiology

[redacted]20[redacted] (Rx Day 335): OTHER TERMINAL ILEUM HISTOCHEMICAL EXAMINATION OF SM: Positive-IBD- CD AND ENDOMETRIOSIS TERMINAL ILEUM; OTHER BIOPSY SPECIMENS FROM SMALL INTESTINE RESECTION IMMUNOHISTOCHEMICAL AND MICROBI: Positive-IN THE WALL OF THE SMALL INTESTINE, THE DEPOSITS OF ENDOMETRIOSIS, WITH POSITIVITY OF ESTROGEN RECEPTORS AND CD 10, FURTHER FISTULIZING FORM OF CD

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 328): ABDOMEN X-RAY:ILEUS LOOPS OF SMALL BOWEL; ECG:NORMAL; 20[redacted] (Rx Day 330): X-RAY OF HEART AND LUNGS:NORMAL; [redacted]20[redacted] (Rx Day 335): HISTOLOGY FINDING FROM ILEOCECAL RESECTION:SEGMENTAL FISTULATING FORM OF CROHN'S DISEASE OF THE SMALL INTESTINE WITH FOCI OF ENDOMETRIOSIS, IMMUNOHISTOCHEMICAL AND POSITIVITY OF ESTROGENIC AND CD 10 RECEPTORS DOC.CHLUMSKA; LAPAROSCOPIS SURGERY OF ABDOMEN-:ILEOCECAL RESECTION BECAUSE THE STENOSIS DUE TO ENDOMETRIOSIS WAS 5 CM BEHINED THE BAUHINI VALVE ,STRICTUROPLASTY DID NOT ALLOW, WE WILL PERFORM MMUNOHISTOLOGICAL EXAMINATION TO CONFIRM ANY ENDOMETRI; RESECTION OF THE ILEOCECAL PART OF THE COLON AND SMALL BOWEL:THE GIT PASSAGE WAS RESTORED WITHOUT COMPLICATIONS

AE Stopped Rx Day	335
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	UNDERLYING DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

Event #4: Serious Adverse Event

Event Description	ENDOMETRIOSIS OF SMALL BOWEL
Preferred Term	子宮内膜症
AE Onset Date / Rx Day	[redacted]20[redacted] / 334
Age at AE Onset	3[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 328): Hematocrit: 0.46 [0.35 - 0.47] FRACTION OF 1; Leukocytes: 33.7 [4 - 10] 10^9/L; [redacted]20[redacted] (Rx Day 329): Albumin: 37 [38 - 58] G/L; C Reactive Protein: 42.5 [0 - 10] MG/L; Hemoglobin: 117 [120 - 160] G/L; Potassium: 4.4 [3.8 - 5.2] MMOL/L

Microbiology
[redacted]20[redacted] (Rx Day 335): OTHER TERMINAL ILEUM HISTOCHEMICAL EXAMINATION OF SM: Positive-IBD- CD AND ENDOMETRIOSIS TERMINAL ILEUM; OTHER BIOPSY SPECIMENS FROM SMALL INTESTINE RESECTION IMMUNOHISTOCHEMICAL AND MICROBI: Positive-IN THE WALL OF THE SMALL INTESTINE, THE DEPOSITS OF ENDOMETRIOSIS, WITH POSITIVITY OF ESTROGEN RECEPTORS AND CD 10, FURTHER FISTULIZING FORM OF CD

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 328): ABDOMEN X-RAY:ILEUS LOOPS OF SMALL BOWEL; ECG:NORMAL; [redacted]20[redacted] (Rx Day 330): X-RAY OF HEART AND LUNGS:NORMAL; [redacted]20[redacted] (Rx Day 335): HISTOLOGY FINDING FROM ILEOCECAL RESECTION:SEGMENTAL FISTULATING FORM OF CROHN'S DISEASE OF THE SMALL INTESTINE WITH FOCI OF ENDOMETRIOSIS, IMMUNOHISTOCHEMICAL AND POSITIVITY OF ESTROGENIC AND CD 10 RECEPTORS DOC.CHLUMSKA; LAPAROSCOPIS SURGERY OF ABDOMEN-:ILEOCECAL RESECTION BECAUSE THE STENOSIS DUE TO ENDOMETRIOSIS WAS 5 CM BEHINED THE BAUHINI VALVE ,STRICTUROPLASTY DID NOT ALLOW, WE WILL PERFORM MMUNOHISTOLOGICAL EXAMINATION TO CONFIRM ANY ENDOMETRI; RESECTION OF THE ILEOCECAL PART OF THE COLON AND SMALL BOWEL:THE GIT PASSAGE WAS RESTORED WITHOUT COMPLICATIONS

AE Stopped Rx Day	341
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	FIBROPTIC STENOSIS OF THE TERMINAL ILEUM
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]

Subject Number: [redacted]

Protocol Number: M16-000

チェコ共和国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，亜イレウス及び亜イレウス悪化の事象を発現した。

Event 1 及び 2 の臨床経過：
関連する病歴は，クローン病，非喫煙者及び非飲酒者であった。

投与 166 日後，被験者は亜イレウスを発現した。投与 297 日後，亜イレウスは消失した。投与 298 日後，被験者は亜イレウス悪化を発現した。投与 301 日後，亜イレウス悪化は消失した。

投与 167 日後，被験者は腹部仙痛，CRP 増加，戦慄，及び胸やけの症状のため入院した。被験者は，少量のエンドウマメ及び人参を繰り返し食べていたことが腸管の通過の妨害となったため，亜イレウスと診断された。投与 173 日後，被験者は退院した。

投与 299 日後，被験者は腹痛及び嘔吐のため入院し，亜イレウス悪化と診断された。補液の再投与後，亜イレウスの症状は消失した。投与 301 日後，被験者は退院し，帰宅した。

投与された薬剤は，Fraxiparine，Metronidazol B，Novalgin，Plasma-Lyte，ソル・メドロール，シプロフロキサシン及び Helicid であった。

The patient's past medications include:

ENTOCORT for CROHN'S DISEASE ([redacted])

PREDNISON for CROHN'S DISEASE ([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

2) 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: Diet mistake.

- AbbVie: Risk factors include pre-existing Crohn's disease and dietary mistake (per PI).

Event of WORSENED SUBILEUS

- Investigator: Underlying disease

- AbbVie: Risk factor includes pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Dilation of long part of ileum.

[redacted] **20[redacted] ABDOMINAL X-RAY:** subileus of small intestinal loops

[redacted] **20[redacted] BILIRUBIN:** 7.4 MMOL/L (normal 3.5 to 21.0)

[redacted] 20[redacted] BODY WEIGHT: 5[redacted] KG

[redacted] 20[redacted] BODY WEIGHT: 5[redacted] KG

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

[redacted] 20[redacted] ECG: normal

[redacted] 20[redacted] ECG: normal

[redacted] **20[redacted] HEMOGLOBIN:** 136 G/L (normal 120 to 160)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 74.6 MG/L (normal 0.0 to 10.0)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 39.8 MG/L (normal 0.0 to 10.0)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 4.4 MG/L (normal 0.0 to 10.0)

[redacted] **20[redacted] URINE KETONES:** 3 no units (normal 0 to 0)

[redacted] **20[redacted] WBC:** 12.4 X10**9/L (normal 4 to 10)

[redacted] **20[redacted] X-RAY ABDOMEN:** Suspection on sub-ileus condition.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

チェコ共和国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，小腸の子宮内膜症及び亜イレウス悪化の事象を発現した。

Event 3及び4の臨床経過：

関連する病歴は，クローン病，炎症性腸疾患（クローン病），非喫煙者及び非飲酒者であった。

投与328日後，被験者は亜イレウス悪化を発現した。投与334日後，被験者は小腸の子宮内膜症を発現した。投与335日後，亜イレウス悪化は消失した。投与341日後，小腸の子宮内膜症は消失した。

投与328日後，被験者は体調が優れず，腹痛，痙攣，悪心，約5回の嘔吐，及び全身状態不良があった。同日，被験者は入院した。被験者は苦痛軽減体位を取ることなく、発熱も認められなかった。被験者はわずかに低カリウム血性であり，MRI小腸造影検査の結果，バウヒン弁の後ろ4 cmのところに狭窄が認められた。腹部X線検査の結果，小腸のイレウスループが認められた。被験者は，コルチコイド及び抗生剤による治療を受けた。しかし，被験者の状態は悪化した。投与335日後，被験者は結腸及び小腸の回盲部の緊急切除を受けた。胃腸管の通過が再開し，合併症は認められなかった。回盲部切除の組織学的検査の所見より，炎症性腸疾患型クローン病に一致する臨床的相関関係が認められた。組織学的検査では，小腸壁に著しい子宮内膜症も認められた（免疫組織化学的検査でエストロゲン，プロゲステロン，CD10陽性）。投与341日後，被験者は退院した。

投与された薬剤は，Novalgin，Sufenta，Fraxiparine及びPlasma-Lyteであった。

The patient was treated with NOVALGIN, SUFENTA, FRAXIPARINE and PLASMALYTE SOLUTION.

he patient's past medications include:

ENTOCORT for CROHN'S DISEASE ([redacted])

PREDNISON for CROHN'S DISEASE ([redacted])

NORMIX for GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Endometriosis of intestine (10014782) (Endometriosis (10014778)) [v.23.1] [10014782]

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

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

Dechallenge: Not Applicable

2) 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 ENDOMETRIOSIS OF SMALL BOWEL

- Investigator: Fibroptic stenosis of the terminal ileum.

- AbbVie: Endometriosis is a common gynecological condition, affecting about 10-15% of women in reproductive age group.

Event of WORSENED SUBILEUS

- Investigator: Underlying disease.

- AbbVie: Risk factors for intestinal stenosis leading to subileus include pre-existing crohn's disease and concurrent intestinal endometriosis. Diagnostics showed stenosis due to intestinal endometriosis as well as restriction due to inflammatory irritation.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMEN X-RAY:** Ileus loops of small bowel

[redacted] 20[redacted] BLOOD PRESSURE: 100/60 mmHg

[redacted] 20[redacted] BODY TEMPERATURE: 36.5 Degrees C

[redacted] 20[redacted] ECG: Normal

[redacted] 20[redacted] ECG: Normal

[redacted] **20[redacted] HEMATOCRIT:** 0.456 fraction of 1 (normal 0.35 to 0.47)

[redacted] **20[redacted] HEMOGLOBIN:** 117 G/L (normal 120 to 160)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 42.5 MG/L (normal 0 to 10)

[redacted] **20[redacted] HISTOLOGY:** Segmental fistulating form of Crohn's disease of the small intestine with foci of endometriosis, immunohistochemical and positivity of estrogenic and CD 10 receptors. Biopsy specimens: in the wall of the small intestine, the deposits of endometriosis, with positivity of estrogen receptors and CD 10, further fistulizing form of CD, granulomas were not detected.

[redacted] **20[redacted] HISTOLOGY:** Small bowel: IBC-CD and Endometriosis terminal ileum.

[redacted] **20[redacted] LAPAROSCOPY ABDOMINAL:** Ileocecal resection because the stenosis due to endometriosis was 5 cm behind the bauhini valve, stricturoplasty did not allow, we will perform immunohistological examination to confirm any endometriosis in a resection small bowel [redacted] 20[redacted]

[redacted] 20[redacted] LEUKOCYTES: 33.1 X10**9/L

[redacted] 20[redacted] PULSE: 100 beats/min

[redacted] **20[redacted] WHITE BLOOD CELLS:** 33.7 X10**9/L (normal 4 to 10)

[redacted] 20[redacted] X-RAY OF HEART AND LUNGS: 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
クローン病	X	X		

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	2[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: MENINGITIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: HEMIKOLECTOMIA L. DX	20[redacted]
OTHER: PNEUMONIE	20[redacted]
OTHER: QUANTIFERON POSITIV	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	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	FORMER	2 - 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 50	[redacted]20[redacted] / 50	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 148	[redacted]20[redacted] / 148	1

PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 204	[redacted]20[redacted] / 204	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 260	[redacted]20[redacted] / 260	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 315	[redacted]20[redacted] / 315	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 378	[redacted]20[redacted] / 378	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: 19[redacted]
PLASMA LYTE 148	1000 mL	QD	Y-M: 20[redacted] / 16

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
PLASMA LYTE 148	1000 mL	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 393
AMINO ACIDS NOS W/CALCIUM CHLORIDE/ELECTROLYT	80 OTHER: ML/HOUR	QD	Y-M: 20[redacted] / 382	Y-M: 20[redacted] / 393
METAMIZOLE	1000 mg	PRN	Y-M: 20[redacted] / 382	Y-M: 20[redacted] / 393
NADROPARIN	0.4 mL	QD	Y-M: 20[redacted] / 382	Y-M: 20[redacted] / 393
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / 382	Y-M: 20[redacted] / 393
IRON	1 OTHER: AMPULA	QD	Y-M: 20[redacted] / 386	Y-M: 20[redacted] / 386
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 393	ONGOING
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 393

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

Event Description WORSENING OF CROHN'S DISEASE
Preferred Term クローン病
AE Onset Date / Rx Day [redacted]20[redacted] / 382 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset 2[redacted]
Laboratory Testing
[redacted]20[redacted] (Rx Day 382): C Reactive Protein: 210 [0 - 10] MG/L; Erythrocytes: 5.1 [4 - 5.8] 10^12/L; Glucose: 5.8 [3.5 - 6.1] MMOL/L; Hematocrit: 0.38 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 123 [135 - 175] G/L; Leukocytes: 9.9 [3.9 - 11] 10^9/L; NPTST537-UREA: 2.6 [3 - 7.4] MMOL/L; Platelets: 273 [150 - 400] 10^9/L; Potassium: 3.8 [3.8 - 5.2] MMOL/L; Protein: 70 [64 - 80] G/L; Sodium: 136 [133 - 148] MMOL/L; [redacted]20[redacted] (Rx Day 383): NPTST449-QUANTOFERON ELISA: NEGATIVE [0 - 0] IU/mL

Microbiology
[redacted]20[redacted] (Rx Day 382): STOOL C. DIFF.: Positive-AG CLOSTRIDIUM DIFFICILE; OTHER NASOPHARYNGEAL SWAB COVID-19 PCR: Negative; URINE CULTIVATION: Negative; STOOL CULTURE: Negative; BLOOD HEMOCULTURE: Negative; STOOL RECTAL SWAB: Negative-NORMAL FLORA; STOOL TOXIN C. DIFF.: Negative; [redacted]20[redacted] (Rx Day 383): BLOOD HEMOCULTURE: Negative; BLOOD QUANTIFERON ELISA: Negative; [redacted]20[redacted] (Rx Day 385): STOOL CULTIVATION: Negative; STOOL PARAZITOLOGY - GIARDIA LAMBLIA,: Negative; [redacted]20[redacted] (Rx Day 392): OTHER NASOPHARYNGEAL SWAB COVID-19 PCR: Positive-CORONAVIRUS

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 382): ECG:NORMAL; US OF ABDOMEN:WITHOUT PATHOLOGICAL FINDINGS; X-RAY:USUAL FINDING, STATUS POST HEMOCOLECTOMY - STATUS FROM [redacted]20[redacted]; [redacted]20[redacted] (Rx Day 383): CT OF ABDOMEN:LYMPHADENOPATHY OF MESENTERIUM AROUND ANASTOMOSIS, FLUID BETWEEN OF SMALL INTESTINE AND BEHIIND THE BLADDER; [redacted]20[redacted] (Rx Day 387): ESOPHAGOGASTRODUODENOSCOPIC EXAMINATION:MUCOSA IN THE LOWER THIRD OF THE ESOPHAGUS WITH ULCERS

AE Stopped Rx Day	393 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	YERSINIA ENTEROCOLITICA SUPERINFECTION WAS ONLY POSSIBLE CAUSE OF EVENT WHICH WAS NOT CONFIRMED
Discontinued Study Drug Due to the Event	YES
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

チェコ共和国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，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，左半結腸切除，非喫煙者及び元アルコール摂取であった。

投与 382 日後，被験者はクローン病悪化を発現した。投与 393 日後，クローン病悪化は消失した。

投与 382 日後，被験者は臍周囲の鋭い腹痛，悪寒，及び体温 38.6°C のため入院した。被験者は複数の検査を受け，胃下部 1/3 及び十二指腸球部のクローン病と診断された。投与 392 日後，被験者の COVID-19 の検査結果は陽性であった。投与 393 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，Nutridrink，Ciplox，Entizol，Fraxiparine，Metronidazol B.Braun，prednisone，Plasma-Lyte，Novalgin，ソル・メドロール，Oliclinomel，Controloc 及び Nolpaza であった。

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: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of WORSENING OF CROHN'S DISEASE

- Investigator: YERSINIA ENTEROCOLITICA SUPERINFECTION WAS ONLY POSSIBLE CAUSE OF EVENT WHICH WAS NOT CONFIRMED

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **C DIFF:** Stool: Positive for AG Clostridium Difficile

[redacted] **COVID-19 PCR TEST:** Nasopharyngeal Swab: Negative

[redacted] **20[redacted] COVID-19 PCR TEST:** Nasopharyngeal Swab: Positive for Coronavirus

[redacted] **20[redacted] CT OF ABDOMEN:** Lymphadenopathy of mesenterium around anastomosis, fluid between of small intestine and behind the bladder.

[redacted] 20[redacted] ECG: Normal

[redacted] **20[redacted] ESOPHAGOGASTRODUODENOSCOPIC EXAMINATION:** Mucosa in the lower third of the esophagus with ulcers

[redacted] **20[redacted] GLUCOSE:** 5.84 MMOL/L (normal 3.5 to 6.1)

[redacted] **20[redacted] HEMATOCRIT:** 37.7 % (normal 40.0 to 50.0)

[redacted] 20[redacted] HEMOCULTURE: Negative

[redacted] 20[redacted] HEMOCULTURE: Negative

[redacted] **20[redacted] HEMOGLOBIN:** 123 G/L (normal 135 to 175)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 142.2 MG/L (normal 0 to 10)

[redacted] **20[redacted] PLATELET COUNT:** 273 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] POTASSIUM:** 4.07 MMOL/L (normal 3.8 to 5.2)

[redacted] **20[redacted] PROTEIN:** 70.3 G/L (normal 64 to 80)

[redacted] 20[redacted] RECTAL SWAB: NORMAL FLORA

[redacted] **20[redacted] RED BLOOD CELLS:** 5.11 X10**12/L (normal 4.0 to 5.8)

[redacted] **20[redacted] SODIUM:** 136.8 MMOL/L (normal 133 to 148)

[redacted] 20[redacted] STOOL CULTIVATION: Negative

[redacted] 20[redacted] STOOL CULTURE: Negative

[redacted] 20[redacted] STOOL PARAZITOLOGY - GIARDIA LAMBLIA, ENTAMOEB: NEGATIVE

[redacted] 20[redacted] TOXIN C. DIFF: Stool: Negative

[redacted] **20[redacted] UREA:** 2.6 MMOL/L (normal 3.0 to 7.4)

[redacted] 20[redacted] URINE CULTIVATION: Negative

[redacted] **20[redacted] US OF ABDOMEN:** Without pathological findings.

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9.9 X10**9/L (normal 3.9 to 11)

[redacted] **20[redacted] X-RAY:** Usual finding, status post hemocolectomy. Status from [redacted] 20[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
尿中ビリルビン増加				X
ウイルス感染	X			X

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	3[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: SEASONAL ALLERGIES	NOT REPORTED
INFLAMMATORY BOWEL DISEASE: CROHNS DISEASE	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: ANGIO OEDEMA	20[redacted]
OTHER: CHRONIC SPONTANEOUS URTICARIA	20[redacted]
OTHER: DERMATOGRAPHISM	20[redacted]

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	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1

M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	20[redacted] / 57	20[redacted] / 57	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 57	20[redacted] / 57	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 80	20[redacted] / 80	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 141	20[redacted] / 141	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 197	20[redacted] / 197	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 253	20[redacted] / 253	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 309	20[redacted] / 309	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: 19[redacted]
INFLIXIMAB	350 mg	Q2M	Y-M: 20[redacted]
INFLIXIMAB	350 mg	Q2M	Y-M: 20[redacted]
ADALIMUMAB	160 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	160 mg	OTHER: INDUCTION DOSE	Y-M: 20[redacted]
ADALIMUMAB	80 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	80MG mg	OTHER: WEEK 2 INDUCTION	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: MAINTENANCE 2 WEEKLY	Y-M: 20[redacted]
FEXOFENADINE	360 mg	QD	Y-M: 20[redacted] / 18
MONTELUKAST	10 mg	PRN	Y-M: 20[redacted] / 48
PANADEINE CO	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 48

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
PANADEINE CO	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 343
CODEINE	30MG mg	NOT REPORTED	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 116
MORPHINE	UN mg	NOT REPORTED	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 116
TRAMADOL	UNK mg	NOT REPORTED	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 116

NEFOPAM	UN mg	NOT REPORTED	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 122
PARACETAMOL	UNK mg	PRN	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 343
BENZYDAMINE	0.15% uL	PRN	Y-M: 20[redacted] / 111	Y-M: 20[redacted] / 343
CETIRIZINE	10 mg	BID	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 343
CROMOGLICIC ACID	1O mL	QID	Y-M: 20[redacted] / 231	ONGOING
BENZACLIN TOPICAL	10MG/50MG mg	PRN	Y-M: 20[redacted] / 357	ONGOING

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

Event Description	VIRAL INFECTION
Preferred Term	ウイルス感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 106
Age at AE Onset	3[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
[redacted]20[redacted] (Rx Day 111): BLOOD BLOOD CULTURES: Negative; CEREBROSPINAL FLUID LUMBAR PUNCTURE: Negative; OTHER THROAT SWAB VIRAL THROAT SWAB: Negative

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 111): CT SCAN HEAD:NORMAL; LUMBAR PUNCTURE:NORMAL; OTOSCOPY:NORMAL

AE Stopped Rx Day	137
Duration of AE	32 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	VIRAL INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Hepatic Events

Event Description	HYPERBILIRUBIN IN URINE DIP
Preferred Term	尿中ビリルビン増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 309
Age at AE Onset	3[redacted]

Laboratory Testing
NOT APPLICABLE

Microbiology
NOT APPLICABLE

SAE Supplemental Procedure
NOT APPLICABLE

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

Generated: [redacted]20[redacted]:09:28
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

英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 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，ウイルス感染の事象を発現した。

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 杯未満）であった。

投与 106 日後，被験者はウイルス感染を発現した。

投与 110 日後，被験者は入院した。同日，被験者は頭痛及び頚部痛の非重篤事象も発現した。被験者は，腰椎穿刺を受けた結果，陰性であった。CSF 検査の結果は正常で，微生物学的及びウイルス学的検査結果は陰性であった。血液培養及びウイルス性咽頭スワブ検査の結果も正常であった。被験者は，頚部痛がコデイン，paracetamol，トラマドール及び Oramorph で改善しなかったと報告した。被験者は，Co-codamol による両腕及び両手のピリピリ感を報告した。被験者の症状は nefopam によって改善し，退院可能と判断された。投与 117 日後，被験者は退院した。

投与された薬剤は，paracetamol，コデイン，アモキシシリン，nefopam，Oramorph 及びトラマドールであった。

The patient's past medications include:

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

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

Causality for ABBV-066 (Blinded)

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1) Viral infection (10047461) (Viral infection (10047461)) [v.21.1] [10047461]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABBV-066 (Blinded)

Event of VIRAL INFECTION

- Investigator: VIRAL INFECTION

- AbbVie: Event is common in the general population

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD CULTURES: Negative

[redacted] 20[redacted] CEREBROSPINAL FLUID: Lumbar puncture-Negative

[redacted] 20[redacted] CSF CULTURE: Negative

[redacted] 20[redacted] HEAD CT SCAN: Normal

[redacted] 20[redacted] OTOSCOPY: Normal

[redacted] 20[redacted] VIRAL THROAT SWAB: Negative

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ＣＯＶＩＤ－１９	X			X

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	4[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	19[redacted]
OTHER: PERIPHERAL ARTHROPATHY	19[redacted]
LIVER DISEASE (EXCLUDING HEPATITIS): GILBERT DISEASE	20[redacted]
ANEMIA: IRON DEFICIENCY	20[redacted]
OTHER: GALLSTONES	20[redacted]
OTHER: NEUTROPENIC SEPSIS FROM AZATHIOPURINE	20[redacted]
OTHER: PERIPHERAL VASCULAR DISEASE	20[redacted]
OTHER: FOLLICULITIS	20[redacted]
OTHER: ACID REFLUX	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: RIGHT HEMI-COLECTOMY	19[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	15 CIGARETTE	6	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1

M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	20[redacted] / 29	20[redacted] / 29	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 29	20[redacted] / 29	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	20[redacted] / 57	20[redacted] / 57	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 57	20[redacted] / 57	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 92	20[redacted] / 92	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 148	20[redacted] / 148	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 207	20[redacted] / 207	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 263	20[redacted] / 263	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 322	20[redacted] / 322	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	20[redacted] / 345	20[redacted] / 345	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 378	20[redacted] / 378	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 441	20[redacted] / 441	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted] / -18

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
NOT REPORTED				

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

Event Description COVID-19 INFECTION
Preferred Term ＣＯＶＩＤ－１９
AE Onset Date / Rx Day [redacted]20[redacted] / 411
Age at AE Onset 5[redacted]
Laboratory Testing
[redacted]20[redacted] (Rx Day 410): Leukocytes: 7.9 [4.3 - 11.2] 10^9/L; NPTST531-TROPONIN: 5 [5 - 34] MM/H; Neutrophils: 6.2 [1.9 - 7.9] 10^9/L
Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 410): CHEST X RAY:CLEAR; ELECTROCARDIOGRAM (ECG):SINUS RHYTHM - NO CONCORDANT ST CHANGES

AE Stopped Rx Day	421
Duration of AE	11 DAYS
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	COVID-19 INFECTION FROM POSSIBLE WORKPLACE
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

英国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及びリサンキズマブが投与され，COVID-19 感染の事象を発現した。

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 15 本を 6 年間），アザチオプリンによる好中球減少性敗血症，末梢血管疾患，呑酸及び飲酒者（1 日 2 杯未満）であった。

20[redacted]年[redacted]月[redacted]日，レスキュー治療としてリサンキズマブの非盲検投与が開始された。

投与 411 日後，被験者は COVID-19 感染を発現した。

投与 410 日後，被験者は，1 時間継続した胸痛，疲労，不安及び浮動性めまいのため入院した。胸部 X 線検査，ECG 及びトロポニン値が入手され，その結果は正常であった。COVID-19 の鼻咽頭スワブ検査の結果は陽性であった。入院中，合併症の発現はなかった。投与 411 日後，被験者は退院し，胸痛は発現していなかった。

被験者には臨床的追跡調査は行われなかった。胸痛は，SAR-COV2 のゴールドスタンダードである PCR 鼻咽頭スワブ検査で確認された COVID-19 感染に関連していると判断された。退院以降の被験者の呼吸数は 18 回／分，酸素飽和度は室内気下で 99%であった。CT スキャン検査

は行われなかった。

追跡調査が行われ，前回報告された胸痛の事象は重篤な事象から除外された。投与 421 日後，COVID-19 感染は消失した。

Causality for RISANKIZUMAB (Blinded)

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1) COVID-19 (10084268) (COVID-19 (10084268)) [v.23.1] [10084268]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

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1) COVID-19 (10084268) (COVID-19 (10084268)) [v.23.1] [10084268]

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 COVID-19 INFECTION

- Investigator: Covid-19 infection from possible workplace.

- AbbVie: Event is more likely related to the COVID-19 pandemic outbreak.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of COVID-19 INFECTION

- Investigator: Covid-19 infection from possible workplace.

- AbbVie: Event is more likely related to the COVID-19 pandemic outbreak.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CHEST X RAY: CLEAR

[redacted] **20[redacted] COVID-19 VIRUS TEST:** nasopharyngeal swab: positive

[redacted] **20[redacted] ELECTROCARDIOGRAM:** SINUS RHYTHM - NO CONCORDANT ST CHANGES

[redacted] **20[redacted] NEUTROPHIL:** 5.51 GI/L (normal 1.96 to 7.23)

[redacted] **20[redacted] NEUTROPHIL:** 4.61 GI/L (normal 1.96 to 7.23)

[redacted] **20[redacted] NEUTROPHIL:** 6.98 GI/L (normal 1.96 to 7.23)

[redacted] **20[redacted] NEUTROPHIL:** 4.55 GI/L (normal 1.96 to 7.23)

[redacted] **20[redacted] NEUTROPHIL:** 5.34 GI/L (normal 1.96 to 7.23)

[redacted] **20[redacted] NEUTROPHIL:** 3.86 GI/L (normal 1.96 to 7.23)

[redacted] **20[redacted] NEUTROPHIL:** 6.2 X10**9/L (normal 1.9 to 7.9)

[redacted] 20[redacted] OXYGEN SATURATION: 99% on room air

[redacted] 20[redacted] RESPIRATORY RATE: 18 /min

[redacted] **20[redacted] TROPONIN:** < 5 mm/h (5 to 34)

[redacted] **20[redacted] WBC:** 7.63 GI/L (normal 3.8 to 10.7)

[redacted] **20[redacted] WBC:** 6.69 GI/L (normal 3.8 to 10.7)

[redacted] **20[redacted] WBC:** 9.31 GI/L (normal 3.8 to 10.7)

[redacted] **20[redacted] WBC:** 6.22 GI/L (normal 3.8 to 10.7)

[redacted] **20[redacted] WBC:** 7.27 GI/L (normal 3.8 to 10.7)

[redacted] **20[redacted] WBC:** 5.73 GI/L (normal 3.8 to 10.7)

[redacted] **20[redacted] WBC:** 7.9 X10**9/L (normal 4.3 to 11.2)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ウイルス感染	X			X

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
ANEMIA: IRON DEFICIENCY ANAEMIA	20[redacted]
OTHER: PERIPHERAL ARTHROPATHY	20[redacted]
OTHER: VITAMIN D DEFICIENCY	20[redacted]
OTHER: BILE ACID MALABSORPTION	20[redacted]
OTHER: FOLIC ACID DEFICIENCY	20[redacted]
OTHER: ANKYLOSING SPONDYLITIS	20[redacted]
OTHER: ANAL FISSURE	20[redacted]

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	FORMER	10 CIGARETTE	8	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 88	[redacted]20[redacted] / 88	1

M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 88	[redacted]20[redacted] / 88	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 115	[redacted]20[redacted] / 115	1
M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 140	[redacted]20[redacted] / 140	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 140	[redacted]20[redacted] / 140	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 172	[redacted]20[redacted] / 172	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 225	[redacted]20[redacted] / 225	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 289	[redacted]20[redacted] / 289	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 339	[redacted]20[redacted] / 339	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 393	[redacted]20[redacted] / 393	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 451	[redacted]20[redacted] / 451	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 507	[redacted]20[redacted] / 507	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]
LEKOVIT CA	CALCIUM 15MMOL & VITAMIN D 400 UNITS OTHER: MMOL/UNIT	QD	Y-M: 20[redacted]
ADALIMUMAB	160 mg	OTHER: ONCE ONLY LOADING DOSE	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: ONCE ONLY LOADING DOSE	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
CONTRACEPTIVES	68 mg	OTHER: 3 YEARLY	Y-M: 20[redacted] / -288
ALL OTHER NON-THERAPEUTIC PRODUCTS	N/A OTHER: N/A	PRN	Y-M: 20[redacted] / 91

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
CONTRACEPTIVES	68 mg	OTHER: 3 YEARLY	Y-M: 20[redacted] / -288	ONGOING

CODEINE	30 mg	QID	Y-M: 20[redacted] / 275	Y-M: 20[redacted] / 277
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 275	Y-M: 20[redacted] / 277
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 275	Y-M: 20[redacted] / 277
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 275	Y-M: 20[redacted] / 284

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

Event Description	VIRAL INFECTION
Preferred Term	ウイルス感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 261
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 275): Leukocytes: 18.4 [4 - 11] 10^9/L; NPTST090-C-REACTIVE PROTEIN: 161 [5 - 5] MG/L; [redacted]20[redacted] (Rx Day 276): NPTST555-VIROLOGY: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (Rx Day 277): Leukocytes: 7.8 [4 - 11] 10^9/L; NPTST090-C-REACTIVE PROTEIN: 73.4 [5 - 5] MG/L

Microbiology

[redacted]20[redacted] (Rx Day 275): URINE MICROBIOLOGY, CULTURE AND SENSI: Negative; [redacted]20[redacted] (Rx Day 276): CEREBROSPINAL FLUID MICROBIOLOGY, CULTURE AND SENSI: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 276): LUMBAR PUNCTURE:MICROBIOLOGY-NO ORGANISM SEEN. VIROLOGY- NEGATIVE

AE Stopped Rx Day	284
Duration of AE	24 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:09:28
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

英国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，ウイルス感染の事象を発現した。

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10本を8年間），強直性脊椎炎及び飲酒者（1日2杯未満）であった。

投与261日後，被験者はウイルス感染を発現した。投与284日後，ウイルス感染は消失した。

投与275日後，被験者は頭痛，頚部硬直及び発熱のため入院した。被験者は髄膜炎に対して腰椎穿刺による精査を受けた。その結果，CSF蛋白値及びCSFブドウ糖値は正常であり，CSFに微生物の増殖は認められず，CSF中WBC値は正常であり，CSFのウイルス学的検査の結果は正常であった。CSFの所見に基づいて，髄膜炎は除外された。しかし，被験者のCRP値及びWBC値は上昇していた。被験者はアモキシシリン・クラブラン酸合剤による治療を受け，及び炎症マーカーの低下傾向が認められた。投与277日後，被験者は退院した。

投与された薬剤は，アモキシシリン・クラブラン酸合剤，コデインリン酸塩及びparacetamolであった。

The patient's past medications include:

ADALIMUMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Viral infection (10047461) (Viral infection (10047461)) [v.23.0] [10047461]

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 VIRAL INFECTION

- Investigator: Not applicable

- AbbVie: Viral infection is nonspecific and common in the general population and can result in the symptoms of headache, neck stiffness, and fever.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] C-REACTIVE PROTEIN: 161.0 MG/L (normal <5)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 73.4 MG/L (normal <5)

[redacted] **20[redacted] CSF CULTURE:** MICROBIOLOGY-NO ORGANISM SEEN. VIROLOGY- NEGATIVE

[redacted] 20[redacted] CSF GLUCOSE: Normal

[redacted] 20[redacted] CSF PROTEIN: Normal

[redacted] 20[redacted] CSF WBC: normal

[redacted] 20[redacted] URINE CULTURE: Negative

[redacted] 20[redacted] VIRAL TEST CSF: Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 18.35 X10**9/L (normal 4.00 to 11.00)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.76 X10**9/L (normal 4.00 to 11.00)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	5[redacted]	MALE	WHITE

Medical History	Onset Year
OSTEOARTHRITIS: ARTHROPATHY	NOT REPORTED
OTHER: POLLEN ALLERGY	NOT REPORTED
MIGRAINE HEADACHE: RECURRING MIGRAINE	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: IRON DEFICIENCY	20[redacted]
NEPHROLITHIASIS: RECURRING KIDNEY STONES	20[redacted]
OTHER: DRY SKIN BOTH LOWER LEGS	20[redacted]

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	CURRENT	11 CIGARETTE	30	
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)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85	1

PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 144 144	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 197 197	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 253 253	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 309 309	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 365 365	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 421 421	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
THOMAPYRIN N	1 OTHER: TABLET	PRN	Y-M: 20[redacted]
SUMATRIPTAN	UNK mg	PRN	Y-M: 20[redacted]
BISOPROLOL	5 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -55
NEBIVOLOL	5 mg	QD	Y-M: 20[redacted] / 73

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
THOMAPYRIN N	1 OTHER: TABLET	PRN	Y-M: 20[redacted]	NOT REPORTED
BISOPROLOL	5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 103
NEBIVOLOL	5 mg	QD	Y-M: 20[redacted] / 73	Y-M: 20[redacted] / 441
IBUPROFEN	400 mg	PRN	Y-M: 20[redacted] / 140	Y-M: 20[redacted] / 142
METAMIZOLE	20 mg	PRN	Y-M: 20[redacted] / 140	Y-M: 20[redacted] / 142

Event #1: Serious Adverse Event

Event Description	KIDNEY STONE
Preferred Term	腎結石症
AE Onset Date / Rx Day	[redacted]20[redacted] / 130
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 140): Erythrocytes: 72000 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 3000 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST041-BACTERIA: FEW [0 - 0] UNIT NOT REPORTED; NPTST066-BLOOD: 5+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST137-COLOR: AMBER [NOT REPORTED - NOT