Subject Number: [redacted]

Protocol Number: M16-000

米国の治験責任医師からの報告。本被験者は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及びリサンキズマブが投与され，播種性ヒストプラスマ症の事象を発現した。

Event 1の臨床経過：

関連する病歴は，慢性疾患の貧血，間欠性脱水，クローン病，急性腎不全，詳細不明急性腎不全（HCC），高血圧，非喫煙者，非飲酒者，大腸炎，血便排泄，急性失血性貧血，直腸出血を伴うクローン病増悪（HCC），合併症のない結腸クローン病（HCC）及び結腸内視鏡検査であった。

被験者は，20[redacted]年[redacted]月[redacted]日から20[redacted]年[redacted]月[redacted]日まで盲検化された治験薬が投与され，20[redacted]年[redacted]月[redacted]日，非盲検化されたリサンキズマブによるレスキュー治療を受けた。

投与460日後，被験者は播種性ヒストプラスマ症を発現した。

治験薬の最終投与は投与431日後であった。

投与460日後，被験者は定期検査である結腸内視鏡検査を受け，治験責任医師によって結腸全体に複数の偽ポリープの存在が確認された。一部のポリープは切除され，病理組織学的分析が行われた。分析の結果，結腸粘膜組織上にヒストプラスマ様生物が示唆される真菌胞子の顕著な関与の存在が明らかになった。被験者によると，被験者はクローン病の消化管症状の治療についてベースラインの状態にあった。また，ほぼ毎日5回の軟便の排泄があり，血便の場合もあった。被験者に皮膚病変はなかった。パラフィンブロックA4でPAS染色及びメテナミン銀染色を行い，多数の真菌胞子の存在が確認された。感染症医の診察の結果，被験者は消化管における播種性ヒストプラスマ症と診断された。抗真菌薬の投与が開始された。投与475日後の時点で，被験者にヒストプラスマ感染の継続を示す徴候は認められなかった。

投与された薬剤は，硫酸鉄，アセトアミノフェン及びイトラコナゾールであった。

The patient's past medications include:

VEDOLIZUMAB for CROHN'S DISEASE ([redacted])

PREDNISONE for CROHN'S DISEASE ([redacted])

CODEINE for UNKNOWN INDICATION

MORPHINE for UNKNOWN INDICATION

PENICILLIN for UNKNOWN INDICATION

Causality for RISANKIZUMAB (Blinded)

---

1) Disseminated histoplasmosis (10013440) (Histoplasmosis disseminated (10020144)) [v.24.0] [10013440]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

---

1) Disseminated histoplasmosis (10013440) (Histoplasmosis disseminated (10020144)) [v.24.0] [10013440]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of DISSEMINATED HISTOPLASMOSIS

- Investigator: Not applicable

- AbbVie: Not applicable

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of DISSEMINATED HISTOPLASMOSIS

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD FUNGAL CULTURE: Negative

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

20[redacted] BMI: 24.74 kg/m2

20[redacted] BODY WEIGHT: 16[redacted] pounds (7[redacted] kg)

20[redacted] CBC AND DIFFERENTIAL: Not reported

[redacted] **20[redacted] COLON, MUCOSAL BIOPSY:** Features consistent with active inflammatory bowel disease. Features of active idiopathic inflammatory bowel disease are present. The overall pattern suggests the possibility of Crohn's disease. Clinical and endoscopic correlation is warranted. Final 1.Inflammatory pseudo-polyps, with some polyps showing surface erosion and marked involvement by fungal spores suggestive of histoplasma. 2.PAS and silver methenamine stains were performed on paraffin block A4 for confirmation of the fungal organisms. Gross description: The specimen is colon polyps consisting of multiple brown pieces of tan-brown, polypoid soft tissue. They range from 0.7 to 2.5x2.0x1.4 cm in greatest dimension. There are 11 pieces total. The 3 smallest pieces each bisected and submitted for double cuts in cassette A2. The largest pieces are marked green, blue, black, red, and gold. The four smaller pieces are each bisected and submitted for double cuts in their own cassettes in cassettes A3-A6. the largest piece is subdivided and submitted for double cuts in cassettes A7-A8. Sections examined microscopically and confirmed the above diagnosis. Numerous fungal spores seen.

[redacted] **20[redacted] COLONOSCOPY:** No pseudopolyps and no suggestion of histoplasma.

[redacted] **20[redacted] COLONOSCOPY:** Showed ulcerations but no pseudo polyps.

[redacted] **20[redacted] COLONOSCOPY:** Active inflammation within the rectum with congested, erythematous and eroded mucosa in the rectum. Other than pseudopolyps there was mild inflammation with erythema (no erosions or ulcers) within the transverse colon; pseudopolyps from transverse colon to rectum.

20[redacted] COMPREHENSIVE METABOLIC PANEL: Not reported

[redacted] **20[redacted] ENDOSCOPY:** Features of active idiopathic inflammatory bowel disease are present. The overall pattern suggests the possibility of Crohn's disease.

[redacted] **20[redacted] FUNGITELL:** 56 PG/ML (normal <80)

[redacted] **20[redacted] GRAM STAIN, PAS, AND SILVER METHENAMINE S:** COLONIC MUCOSA: Positive; Numerous fungal spores seen; inflammatory pseudopolyps, with some polyps showing surface erosion and marked involvement by fungal spores suggestive of histoplasma like organisms. Pas and silver methenamine

stains were performed on paraffin block A4 for confirmation of the fungal organisms.

[redacted] **20[redacted] HEMOGLOBIN:** 8.3 G/DL (normal 13.5 to 17.5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 1.1 mg/dL (normal <0.9)

[redacted] 20[redacted] HISTOPLASMA GALACTOMANNAN ANTIGEN (BLOOD): 0.5 NG/ML (normal <0.5)

[redacted] 20[redacted] HISTOPLASMA GALACTOMANNAN ANTIGEN (URINE): 0.5 NG/ML (normal <0.5)

[redacted] **20[redacted] MONOCYTES %:** 9.8 % (normal 2 to 9)

[redacted] 20[redacted] PULSE: 64 bpm

[redacted] 20[redacted] RESPIRATORY RATE: 16 /min

[redacted] **20[redacted] SED RATE:** 31 MM/HR (normal <15)

[redacted] 20[redacted] T-SPOT TB TEST: Negative

[redacted] 20[redacted] TEMPERATURE: 98.7 F

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			
小腸閉塞	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Placebo SC Q8W	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ASTHMA	20[redacted]
OTHER: CHRONIC HEADACHES	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: OVERACTIVE BLADDER	20[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
OTHER: STREP THROAT	20[redacted]

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

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1

PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 94 94	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 148 148	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 204 204	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 260 260	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 267 267	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 316 316	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 372 372	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	20[redacted] / 20[redacted] / 431 431	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
INFLIXIMAB	10 mg/kg	OTHER: Q 6 WKS	Y-M: 20[redacted]
MIRABEGRON	30 mg	QD	Y-M: 20[redacted] / -193
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -14
FLUTICASONE	1 OTHER: SPRAY	PRN	Y-M: 20[redacted] / 84

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / 112	NOT REPORTED
TRANEXAMIC ACID	650 mg	OTHER: 2 TABLETS 3X/DAY DURING MENSTRUAL CYCLE	Y-M: 20[redacted] / 172	NOT REPORTED
FLUOXETINE	20 mg	QD	Y-M: 20[redacted] / 183	NOT REPORTED
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 255	NOT REPORTED
ALUMINIUM W/MAGNESIUM HYDROXIDE/SIMETICONE	30 mL	PRN	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 414
DOCOSANOL	10 %	PRN	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 414
DOCUSATE W/SENNA	8.6-50 mg	BID	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 414
MORPHINE	2 mg	PRN	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 414

PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 414
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 414
IBUPROFEN	400 mg	PRN	Y-M: 20[redacted] / 411	Y-M: 20[redacted] / 414
PROCHLORPERAZINE	5 mg	PRN	Y-M: 20[redacted] / 411	Y-M: 20[redacted] / 414
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 413	Y-M: 20[redacted] / 413
LIDOCAINE	1 OTHER: PATCH	PRN	Y-M: 20[redacted] / 413	Y-M: 20[redacted] / 414
CURCUMA LONGA	2 OTHER: TABLETS	QD	Y-M: 20[redacted] / 416	NOT REPORTED
PROBIOTICS	2 OTHER: TABLETS	QD	Y-M: 20[redacted] / 416	NOT REPORTED
CLAVULANIC ACID	125 mg	BID	Y-M: 20[redacted] / 466	Y-M: 20[redacted] / 473
BARIUM	1300 mL	OTHER: ONCE	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 479
IOPAMIDOL	75 mL	OTHER: ONCE	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 479
DIAZEPAM	2 mg	PRN	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 480
KETOROLAC	15 mg	PRN	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 480
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 480
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 481
MACROGOL	17 g	QD	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 482
OXYCODONE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 480
MAGNESIUM HYDROXIDE	2400 mg	QD	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 481
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 481
TRAZODONE	50 mg	PRN	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 481
DOCUSATE W/SENNA	8.6-50 mg	BID	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 482
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 482
OXYCODONE	5 mg	BID	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 483

Event #1: Serious Adverse Event

Event Description	SMALL BOWEL OBSTRUCTION
Preferred Term	小腸閉塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 409
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 409): Basophils: 0.04 [0 - 0.3] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 2] %; Eosinophils: 0.12 [0 - 0.5] 10^9/L; Eosinophils/Leukocytes: 0.8 [1 - 4] %; Ery. Mean Corpuscular Hemoglobin: 25.4 [26 - 34] PG; Ery. Mean Corpuscular Volume: 80.3 [80 - 100] FL; Erythrocytes: 4.7 [4 - 5.2] 10^12/L; Hematocrit: 0.38 [0.36 - 0.46] FRACTION OF 1; Hemoglobin: 120 [120 - 160] G/L; Leukocytes: 15.9 [4.5 - 11] 10^9/L; Lymphocytes: 2.71 [0.9 - 4] 10^9/L; Lymphocytes/Leukocytes: 17.1 [20 - 44] %; Monocytes: 0.83 [0.3 - 0.9] 10^9/L; Monocytes/Leukocytes: 5.2 [2 - 9] %; NPTST293-IG ABSOLUTE: 0.06 [0 - 0.3] K/MCL; NPTST294-IG PERCENT: 0.40 [NOT REPORTED - NOT REPORTED] %; NPTST334-MCHC: 31.6 [31 - 37] G/DL; NPTST337-MEAN PLATELET VOLUME: 12.1 [9 - 15.5] FL; NPTST454-RDW-CV: 14.6 [11.6 - 14.8] %; Neutrophils: 12.12 [1.7 - 7] 10^9/L; Neutrophils/Leukocytes: 76.2 [50 - 70] %; Platelets: 356 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 410): C Reactive Protein: 18.4 [0 - 10] MG/L; NPTST316-LACTIC ACID: 1.3 [0.6 - 2] MMOL/L; NPTST484-SEDIMENTATION RATE: 25 [0 - 20] MM/H; [redacted]20[redacted] (Rx Day 411): Ery. Mean Corpuscular Hemoglobin: 25.5 [26 - 34] PG; Ery. Mean Corpuscular Volume: 82 [80 - 100] FL; Erythrocytes: 4.4 [4 - 5.2] 10^12/L; Hematocrit: 0.36 [0.36 - 0.46] FRACTION OF 1; Hemoglobin: 112 [120 - 160] G/L; Leukocytes: 10.3 [4.5 - 11] 10^9/L; NPTST334-MCHC: 31.1 [31 - 37] G/DL; NPTST337-MEAN PLATELET VOLUME: 12.4 [9 - 15.5] FL; NPTST454-RDW-CV: 14.5 [11.6 - 14.8] %; Platelets: 303 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 413): Ery. Mean Corpuscular Hemoglobin: 25.3 [26 - 34] PG; Ery. Mean Corpuscular Volume: 83 [80 - 100] FL; Erythrocytes: 4.3 [4 - 5.2] 10^12/L; Hematocrit: 0.36 [0.36 - 0.46] FRACTION OF 1; Hemoglobin: 109 [120 - 160] G/L; Leukocytes: 9.6 [4.5 - 11] 10^9/L; NPTST334-MCHC: 30.5 [31 - 37] G/DL; NPTST337-MEAN PLATELET VOLUME: 12.4 [9 - 15.5] FL; NPTST454-RDW-CV: 14.5 [11.6 - 14.8] %; Platelets: 280 [150 - 400] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 409): CT ABDOMEN/PELVIS WITH IV CONTRAST:MODERATE CIRCUMFERENTIAL THICKENING INVOLVING THE CECUM AND THE ILEUM CONSISTENT WITH THE PATIENT'S HISTORY OF CROHN'S DISEASE WITH NARROWING OF THE TERMINAL ILEUM, CONCERNING FOR STRICTURE, DILATED L

AE Stopped Rx Day	414
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN'S DISEASE FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	CROHN'S FLARE
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 479 (48 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 479): Alanine Aminotransferase: 18 [0 - 40] U/L; Albumin: 41 [32 - 52] G/L; Alkaline Phosphatase: 60 [40 - 140] U/L; Aspartate Aminotransferase: 13 [0 - 45] U/L; Basophils: 0.03 [0 - 0.3] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 2] %; Blood Urea Nitrogen: 3.9 [2.9 - 8.9] MMOL/L; C Reactive Protein: 8.9 [0 - 10] MG/L; Calcium: 2.25 [2.1 - 2.55] MMOL/L; Chloride: 101 [98 - 108] MMOL/L; Creatinine: 59 [35 - 97] UMOL/L; Eosinophils: 0 [0 - 0.5] 10^9/L; Eosinophils/Leukocytes: 0 [1 - 4] %; Ery. Mean Corpuscular Hemoglobin: 26 [26 - 34] PG; Ery. Mean Corpuscular Volume: 84.6 [80 - 100] FL; Erythrocytes: 4.4 [4 - 5.2] 10^12/L; Glucose: 10.4 [3.6 - 5.5] MMOL/L; Hematocrit: 0.37 [0.36 - 0.46] FRACTION OF 1; Hemoglobin: 115 [120 - 160] G/L; Leukocytes: 10.3 [4.5 - 11] 10^9/L; Lymphocytes: 1.39 [0.9 - 4] 10^9/L; Lymphocytes/Leukocytes: 13.5 [20 - 44] %; Monocytes: 0.24 [0.3 - 0.9] 10^9/L; Monocytes/Leukocytes: 2.3 [2 - 9] %; NPTST028-ANION GAP: 17 [10 - 20] MMOL/L; NPTST060-BICARBONATE: 25 [21 - 32] MMOL/L; NPTST079-BUN/CREATINE RATIO: 16.4 [10 - 20] RATIO; NPTST192-EGFR: 121 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST292-IG ABS: 0.05 [0 - 0.3] K/MCL; NPTST294-IG PERCENT: 0.50 [NOT REPORTED - NOT REPORTED] %; NPTST334-MCHC: 30.7 [31 - 37] G/DL; NPTST358-MPV: 11.4 [9 - 15.5] FL; NPTST380-NUCLEATED RBC: 0 [NOT REPORTED - NOT REPORTED] %; NPTST381-NUCLEATED RBC ABS: 0 [0 - 0] K/MCL; NPTST454-RDW-CV: 14.6 [11.6 - 14.8] %; NPTST484-SEDIMENTATION RATE: 23 [0 - 20] MM/H; NPTST523-TOTAL BILIRUBIN: 0.3 [0 - 1.3] MG/DL; Neutrophils: 8.61 [1.7 - 7] 10^9/L; Neutrophils/Leukocytes: 83.4 [50 - 70] %; Platelets: 287 [150 - 400] 10^9/L; Potassium: 4.2 [3.5 - 5.1] MMOL/L; Protein: 67 [60 - 80] G/L; Sodium: 139 [135 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 479): ABDOMINAL X-RAY:NO BOWEL OBSTRUCTION OR FREE AIR; CHEST X-RAY:LUGS ARE CLEAR WITHOUT ACUTE PROCESS. NO PLEURAL EFFUSION OR PNEUMOTHORAX.; CT ENTEROGRAM WITH CONTRAST:SUBOPTIMAL BOWEL DISTENSION. TRACE INFLAMMATORY CHANGE ABOUT THE TERMINAL ILEUM, DECREASED SINCE [redacted] PERSISTENT THICKENING AT THE TERMINAL ILEUM MAY REFLECT CHRONIC STRICTURE. NO MECHANICAL BOWEL

AE Stopped Rx Day	482 (51 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CHRONIC STRICTURE AT THE ILEOCECAL VALUE AND TERMINAL ILEUM REGION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

米国の治験責任医師からの報告。本被験者は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及びリサンキズマブが投与され，小腸閉塞の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，非喫煙者及び非飲酒者であった。

20[redacted]年[redacted]月[redacted]日，被験者は，非盲検化されたリサンキズマブによるレスキュー治療を受けた。

投与409日後，被験者は小腸閉塞を発現した。

投与409日後，被験者は重度の腹痛，悪心及び嘔吐のため救急治療室を受診し，入院した。CTスキャン及び臨床検査の結果，小腸閉塞と診断された。投与414日後，被験者は退院した。投与414日後，小腸閉塞は消失した。

投与された薬剤は，アセトアミノフェン，モルヒネ，senna-docusate，水酸化マグネシウム／Simeticone，メチルプレドニゾロン酢酸エステル，Percocet，Compazine，プロクロルペラジン，イブプロフェン，リドカイン及びprednisoneであった。

The patient's past medications include:

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

Causality for RISANKIZUMAB (Blinded)

---

1) Small bowel obstruction (10041055) (Small intestinal obstruction (10041101)) [v.23.0] [10041055]

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) Small bowel obstruction (10041055) (Small intestinal obstruction (10041101)) [v.23.0] [10041055]

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 SMALL BOWEL OBSTRUCTION

- Investigator: Crohn's disease flare.

- AbbVie: Event more likely related to pre-existing Crohn's disease and prior cesarean sections (intra-abdominal adhesions).

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of SMALL BOWEL OBSTRUCTION

- Investigator: Crohn's disease flare.

- AbbVie: Event more likely related to pre-existing Crohn's disease and prior cesarean sections (intra-abdominal adhesions).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMEN CT:** moderate circumferential thickening involving the cecum and the ileum consistent with the patient's history of Crohn's disease with narrowing of the terminal ileum, concerning for stricture, dilated loops of small bowel proximally with small-bowel fecalization, concerning for small bowel obstruction.

[redacted] 20[redacted] BASOPHILS: 0.3 %

[redacted] **20[redacted] CRP:** 18.4 MG/L (normal 0.0 to 10.0)

[redacted] **20[redacted] EGFR:** 132 ML/MIN/1.73M2 (normal >60)

[redacted] **20[redacted] EGFR:** 123 ML/MIN/1.73M2 (normal >60)

[redacted] 20[redacted] EOSINOPHILS: 0.8 %

[redacted] **20[redacted] GLUCOSE:** 134 mg/dL (normal 65 to 99)

[redacted] **20[redacted] HEMATOCRIT:** 38.0 % (normal 36.0 to 46.0)

[redacted] **20[redacted] HEMATOCRIT:** 36.0 % (normal 36.0 to 46.0)

[redacted] **20[redacted] HEMATOCRIT:** 35.7 % (normal 36.0 to 46.0)

[redacted] **20[redacted] HEMOGLOBIN:** 12.0 G/DL (normal 12.0 to 16.0)

[redacted] **20[redacted] HEMOGLOBIN:** 11.2 G/DL (normal 12.0 to 16.0)

[redacted] **20[redacted] HEMOGLOBIN:** 10.9 G/DL (normal 12.0 to 16.0)

[redacted] **20[redacted] LACTIC ACID:** 1.3 MMOL/L (normal 0.6 to 2.0)

[redacted] 20[redacted] LYMPHOCYTES: 17.1 %

[redacted] **20[redacted] LYMPHOCYTES ABSOLUTE:** 2.71 K/MCL (normal 0.90 to 4.00)

[redacted] 20[redacted] MONOCYTES: 5.2 %

[redacted] 20[redacted] NEUTROPHILS: 76.2 %

[redacted] **20[redacted] NEUTROPHILS ABSOLUTE:** 12.12 K/MCL (normal 1.70 to 7.00)

[redacted] **20[redacted] PLATELET:** 356 K/MCL (normal 150 to 400)

[redacted] **20[redacted] PLATELET:** 303 K/MCL (normal 150 to 400)

[redacted] **20[redacted] PLATELET:** 280 K/MCL (normal 150 to 400)

[redacted] **20[redacted] SED RATE:** 25 MM/HR (normal 0 to 20)

[redacted] 20[redacted] URINE CULTURE: NEGATIVE

[redacted] **20[redacted] WBC:** 15.88 K/MCL (normal 4.50 to 11.00)

[redacted] **20[redacted] WBC:** 10.33 K/MCL (normal 4.50 to 11.00)

[redacted] **20[redacted] WBC:** 9.62 K/MCL (normal 4.50 to 11.0)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

米国の治験責任医師からの報告。本被験者は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 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。

被験者は，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が投与され，20[redacted]年[redacted]月[redacted]日，非盲検化されたリサンキズマブによるレスキュー治療を受けた。

投与479日後，被験者はクローン病のフレアを発現した。投与482日後，クローン病のフレアは消失した。

投与479日後，被験者は右下腹部疼痛，便秘（4日間排便なし）及び悪心（嘔吐なし）があったため，来院した。画像検査が実施され，被験者は回盲弁及び回腸末端の慢性狭窄によって悪化したクローン病のフレアと診断された。鎮痛薬，コルチコステロイドの静脈内投与及び便軟化薬による治療が行われた。投与482日後，被験者は退院した。

投与された薬剤は，Zofran，メチルプレドニゾロン，ketorolac，アセトアミノフェン，オキシコドン，prednisone及びトラゾドンであった。

The patient's past medications include:

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

PREDNISONE 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)

---

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: NotApplicable

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 CROHN'S FLARE

- Investigator: Chronic stricture at the ileocecal value and terminal ileum region

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

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of CROHN'S FLARE

- Investigator: Chronic stricture at the ileocecal value and terminal ileum region

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL X-RAY:** NO BOWEL OBSTRUCTION OR FREE AIR.

[redacted] **20[redacted] BICARB:** 25 MMOL/L (normal 21 to 32)

[redacted] **20[redacted] CHEST X RAY:** Lungs are clear without acute process. No pleural effusion or pneumothorax.

[redacted] **20[redacted] CHLORIDE:** 101 MMOL/L (normal 98 to 108)

[redacted] **20[redacted] CT ENTEROGRAM WITH CONTRAST:** SUBOPTIMAL BOWEL DISTENSION. TRACE INFLAMMATORY CHANGE ABOUT THE TERMINAL ILEUM, DECREASED SINCE [redacted] PERSISTENT THICKENING AT THE TERMINAL ILEUM MAY REFLECT CHRONIC STRICTURE. NO

MECHANICAL BOWEL OBSTRUCTION.

[redacted] **20[redacted] GLUCOSE:** 187 MMOL/L (normal 65 to 99)

[redacted] **20[redacted] HEMATOCRIT:** 37.4 % (normal 36 to 46)

[redacted] **20[redacted] HEMOGLOBIN:** 11.5 G/DL (normal 12 to 16)

[redacted] **20[redacted] PLT:** 287 K/MCL (normal 150 to 400)

[redacted] **20[redacted] POTASSIUM:** 4.2 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] RBC:** 4.42 K/MCL (normal 4 to 5.2)

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

[redacted] **20[redacted] WBC:** 10.32 K/MCL (normal 36 to 46)

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
胸痛	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	5[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	19[redacted]
OTHER: INTERMITTENT ARTHRALGIAS DUE TO CROHN'S	19[redacted]
OTHER: SEASONAL ALLERGIES	19[redacted]
OTHER: ABDOMINAL PAIN	19[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: GASTRECTOMY	19[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	19[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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 27	[redacted]20[redacted] / 27	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 27	[redacted]20[redacted] / 27	1

M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	20[redacted] / 57	20[redacted] / 57	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 57	20[redacted] / 57	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] / 148	20[redacted] / 148	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 148	20[redacted] / 148	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 204	20[redacted] / 204	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 204	20[redacted] / 204	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 260	20[redacted] / 260	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 260	20[redacted] / 260	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 315	20[redacted] / 315	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 315	20[redacted] / 315	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 372	20[redacted] / 372	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 372	20[redacted] / 372	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 426	20[redacted] / 426	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 426	20[redacted] / 426	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 19[redacted]
CETIRIZINE	10 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
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 19[redacted]	NOT REPORTED
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	NOT REPORTED

ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 139	Y-M: 20[redacted] / 139
ENOXAPARIN	80 mg	OTHER: EVERY 12 HOURS	Y-M: 20[redacted] / 139	Y-M: 20[redacted] / 140

Event #1: Serious Adverse Event

Event Description	CHEST PAIN
Preferred Term	胸痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 132
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 139): Glucose: 8.4 [4.1 - 5.9] MMOL/L; Monocytes/Leukocytes: 12.7 [2 - 11] %; NPTST016-AG RATIO: 0.9 [1.1 - 2.2] RATIO; NPTST254-GLOBULIN (CALC): 4.1 [2.1 - 3.5] G/DL; NPTST333-MAGNESIUM: 1.6 [1.8 - 2.4] MG/DL; [redacted]20[redacted] (Rx Day 140): Creatine Kinase: 308 [21 - 232] U/L; Creatine Kinase: 169 [21 - 232] U/L; NPTST531-TROPONIN: 0.02 [0 - 0.06] NG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 139): CHEST X-RAY:NO ACUTE PULMONARY PROCESS. NO EVIDENCE OF INFILTRATE OR PNEUMONIA; EKG:SINUS RHYTHM, NORMAL EKG; [redacted]20[redacted] (Rx Day 140): STRESS TEST:ABNORMAL STUDY. THERE IS NO EVIDENCE OF TRANSIENT CAVITY DILATATION. NORMAL TRACER DISTRIBUTION. THE LV EF IS CALCULATED AT 48%. THERE IS MILD HYPOKINESIS OF THE GLOBAL WALLS.

AE Stopped Rx Day	140
Duration of AE	9 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	GASTROESOPHAGEAL REFLUX 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

米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が投与され，胸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，胃切除，胃食道逆流性疾患，非喫煙者及び非飲酒者で，胃食道逆流性疾患の家族歴もあった。

投与 132 日後，被験者は胸痛を発現した。投与 140 日後，胸痛は消失した。

投与 139 日後，被験者は投与 132 日後から間欠性胸痛があったため，救急治療室を受診した。心臓の精密検査が行われ，異常は認められなかった。ストレス試験及びトロポニンレベルは正常であった。同日，被験者は入院した。投与 140 日後，被験者は退院した。

投与された薬剤は，酸素，アスピリン及び Lovenox であった。

Causality for RISANKIZUMAB (Blinded)

---

1) Chest pain (10008479) (Chest pain (10008479)) [v.23.1] [10008479]

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 CHEST PAIN

- Investigator: Gastroesophageal reflux disease.

- AbbVie: Event is common in the general population. The mean annual prevalence of noncardiac chest pain in 6 population-based studies was approximately 25%. Additional risk factor includes pre-existing gastroesophageal reflux disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **AG RATIO:** 0.9 RATIO (normal 1.1 to 2.2)

[redacted] **CHEST X-RAY:** No acute pulmonary process. No evidence of infiltrate or pneumonia.

[redacted] **20[redacted] CREATINE KINASE:** 308 U/L (normal 21 to 232)

[redacted] **20[redacted] CREATINE KINASE:** 169 U/L (normal 21 to 232)

[redacted] **20[redacted] EKG:** Sinus Rhythm, normal EKG

[redacted] **20[redacted] GLOBULIN (CALC):** 4.1 G/DL (normal 2.1 to 3.5)

[redacted] **20[redacted] GLUCOSE:** 152 mg/dL (normal 74 to 106)

[redacted] **20[redacted] MAGNESIUM:** 1.6 mg/dL (normal 1.8 to 2.4)

[redacted] **20[redacted] MONOCYTES:** 12.7 % (normal 2.0 to 11.0)

[redacted] **20[redacted] STRESS TEST:** Abnormal study. There is no evidence of transient cavity dilatation. Normal tracer distribution. The LV EF is calculated at 48%. There is mild hypokinesis of the global walls.

[redacted] **20[redacted] TROPONIN:** 0.017 NG/ML (normal 0.0 to 0.056)

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 M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	2[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
MIGRAINE HEADACHE	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: ORAL APHTHOUS ULCERS	20[redacted]
OTHER: GENERALIZED ANXIETY	20[redacted]
OTHER: OSTEOPENIA	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: PLACEMENT OF TOTAL PARENTERAL NUTRITION	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)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 31	[redacted]20[redacted] / 31	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 59	[redacted]20[redacted] / 59	1

M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 87	[redacted]20[redacted] / 87	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 87	[redacted]20[redacted] / 87	1
M16006 /RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 87	[redacted]20[redacted] / 87	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 113	[redacted]20[redacted] / 113	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 141	[redacted]20[redacted] / 141	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 141	[redacted]20[redacted] / 141	1
M16006 /RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 141	[redacted]20[redacted] / 141	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 170	[redacted]20[redacted] / 170	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 170	[redacted]20[redacted] / 170	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 223	[redacted]20[redacted] / 223	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 223	[redacted]20[redacted] / 223	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 282	[redacted]20[redacted] / 282	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 282	[redacted]20[redacted] / 282	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 335	[redacted]20[redacted] / 335	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 335	[redacted]20[redacted] / 335	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 346	[redacted]20[redacted] / 346	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 394	[redacted]20[redacted] / 394	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] / 504	[redacted]20[redacted] / 504	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
MELATONIN	10 mg	QD	Y-M: 20[redacted]
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]
CALCIUM	600 mg	QD	Y-M: 20[redacted]

MERCAPTOPURINE	50 mg	QD	Y-M: 20[redacted] / -137
SERTRALINE	50 mg	QD	Y-M: 20[redacted] / -75

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
IRON	25 mg	QD	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 346
ERGOCALCIFEROL	1.25 mg	QD	Y-M: 20[redacted] / 347	Y-M: 20[redacted] / 347
MAGNESIUM SULFATE	4 g	QD	Y-M: 20[redacted] / 347	Y-M: 20[redacted] / 347
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 347	Y-M: 20[redacted] / 347
PARACETAMOL	500 mg	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 347	Y-M: 20[redacted] / 348
SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 347	Y-M: 20[redacted] / 348
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 347	Y-M: 20[redacted] / 349
HEPARIN	1 mL	QD	Y-M: 20[redacted] / 347	Y-M: 20[redacted] / 349
MELATONIN	6 mg	QD	Y-M: 20[redacted] / 348	Y-M: 20[redacted] / 348
IRON	325 mg	TID	Y-M: 20[redacted] / 349	NOT REPORTED
MAGNESIUM OXIDE	800 mg	QD	Y-M: 20[redacted] / 349	Y-M: 20[redacted] / 349
ERGOCALCIFEROL	1.25 mg	OTHER: EVERY WEEK	Y-M: 20[redacted] / 349	Y-M: 20[redacted] / 391

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF CROHNS
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 346
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 347): Alanine Aminotransferase: 126 [5 - 49] UNIT NOT REPORTED; Albumin: 2.9 [3.5 - 5] UNIT NOT REPORTED; Aspartate Aminotransferase: 155 [5 - 42] UNIT NOT REPORTED; C Reactive Protein: <0.02 [0.02 - 0.5] UNIT NOT REPORTED; Erythrocytes: 4.45 [4.63 - 6.08] UNIT NOT REPORTED; Hematocrit: 33.4 [40.1 - 51] UNIT NOT REPORTED; Hemoglobin: 10.5 [13.7 - 17.5] UNIT NOT REPORTED; Leukocytes: 11.77 [4 - 10.04] UNIT NOT REPORTED; NPTST146-COVID-19: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 255 [163 - 369] UNIT NOT REPORTED; [redacted]20[redacted] (Rx Day 348): Alanine Aminotransferase: 95 [5 - 49] UNIT NOT REPORTED; Albumin: 2.8 [3.5 - 5] UNIT NOT REPORTED; Aspartate Aminotransferase: 83 [5 - 42] UNIT NOT REPORTED; Erythrocytes: 4.30 [4.63 - 6.08] UNIT NOT REPORTED; Hematocrit: 31.6 [40.1 - 51] UNIT NOT REPORTED; Hemoglobin: 10.0 [13.7 - 17.5] UNIT NOT REPORTED; Leukocytes: 7.77 [4 -

10.04] UNIT NOT REPORTED; Platelets: 234 [163 - 369] UNIT NOT REPORTED; [redacted]20[redacted] (Rx Day 349): Alanine Aminotransferase: 70 [5 - 49] UNIT NOT REPORTED; Albumin: 2.9 [3.5 - 5] UNIT NOT REPORTED; Aspartate Aminotransferase: 46 [5 - 42] UNIT NOT REPORTED; Erythrocytes: 4.19 [4.63 - 6.08] UNIT NOT REPORTED; Hematocrit: 31.2 [40.1 - 51] UNIT NOT REPORTED; Hemoglobin: 9.6 [13.7 - 17.5] UNIT NOT REPORTED; Leukocytes: 6.30 [4 - 10.04] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (Rx Day 347): BLOOD CULTURE ROUTINE BLOOD: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 347): CT ABDOMEN AND PELVIS:IMPRESSION: INFLAMED SEGMENTS OF THE COLON COMPATIBLE WITH REPORTED CROHNS DISES. MINIMAL DISTAL SMALL BOWEL ILEUS. NO SMALL BOWEL OBSTRUCTION. RECOMMEND FOLLOW-UP

AE Stopped Rx Day	349
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PROGRESSION OF UNDERLYING 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

米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及びリサンキズマブが投与され，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，胃食道逆流性疾患，中心静脈カテーテル留置，口腔内アフタ性潰瘍，非喫煙者及び非飲酒者であった。

被験者は，20[redacted]年[redacted]月[redacted]日から20[redacted]年[redacted]月[redacted]日まで盲検化された治験薬が投与され，20[redacted]年[redacted]月[redacted]日，非盲検化されたリサンキズマブによるレスキュー治療を受けた。

投与346日後，被験者はクローン病増悪を発現した。投与349日後，クローン病増悪は消失した。

投与 347 日後，被験者は発熱，頭痛及び下痢があったため，救急治療室を受診した。悪心，嘔吐，咽喉痛，鼻漏及び息切れはなかった。左方移動を伴う白血球増加症が認められた。CT 検査の結果，結腸にクローン病に矛盾しない炎症部位及び遠位小腸に軽微なイレウスが認められたが，小腸閉塞は認められなかった。同日，被験者は入院した。まず Cipro 及びフラジールが 1 回投与されたが，その後ゾシンに変更された。ステロイドの投与は行われなかった。被験者に合併症はなく，入院中に手術は行われなかった。投与 349 日後，被験者は退院し，オーグメンチンの経口投与となった。退院時，被験者の体調は良く，症状はほぼ消失していた。

被験者は以前のフレア時にこれらの事象を発現していた。

投与された薬剤は，ゾシン，Cipro，オーグメンチン及びフラジールであった。

Causality for RISANKIZUMAB (Blinded)

---

1) Crohns disease aggravated (10011408) (Crohn's disease (10011401)) [v.22.1] [10011408]

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) Crohns disease aggravated (10011408) (Crohn's disease (10011401)) [v.22.1] [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 EXACERBATION OF CROHNS

- Investigator: Progression of underlying disease.

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

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of EXACERBATION OF CROHNS

- Investigator: Progression of underlying disease.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 126 no units (normal 5 to 49)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 95 no units (normal 5 to 49)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 70 no units (normal 5 to 49)

[redacted] **20[redacted] ALBUMIN:** 2.9 no units (normal 3.5 to 5.0)

[redacted] **20[redacted] ALBUMIN:** 2.8 no units (normal 3.5 to 5.0)

[redacted] **20[redacted] ALBUMIN:** 2.9 no units (normal 3.5 to 5.0)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 155 no units (normal 5 to 42)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 83 no units (normal 5 to 42)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 46 no units (normal 5 to 42)

[redacted] 20[redacted] BODY WEIGHT: 12[redacted] Pounds

[redacted] 20[redacted] COVID-19 (NASOPHARYNGEAL): NEGATIVE

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** IMPRESSION: INFLAMED SEGMENTS OF THE COLON COMPATIBLE WITH REPORTED CROHNS DISES. MINIMAL DISTAL SMALL BOWEL ILEUS. NO SMALL BOWEL OBSTRUCTION. RECOMMEND FOLLOW-UP

[redacted] 20[redacted] CULTURE ROUTINE BLOOD: Negative

[redacted] **20[redacted] HEMATOCRIT:** 33.4 no units (normal 40.1 to 51.0)

[redacted] [redacted] **20**[redacted] **HEMATOCRIT:** 31.6 no units (normal 40.1 to 51.0)

[redacted] [redacted] **20**[redacted] **HEMATOCRIT:** 31.2 no units (normal 40.1 to 51.0)

[redacted] [redacted] **20**[redacted] **HEMOGLOBIN:** 10.5 no units (normal 13.7 to 17.5)

[redacted] [redacted] **20**[redacted] **HEMOGLOBIN:** 10.0 no units (normal 13.7 to 17.5)

[redacted] [redacted] **20**[redacted] **HEMOGLOBIN:** 9.6 no units (normal 13.7 to 17.5)

[redacted] [redacted] **20**[redacted] **HIGH-SENSITIVITY C REACTIVE PROTEIN:** Test result: <0.02 no units Normal value low: 0.02 no units Normal value high: 0.50 no units

[redacted] [redacted] **20**[redacted] **PLATELET COUNT:** 255 no units (normal 163 to 369)

[redacted] [redacted] **20**[redacted] **PLATELET COUNT:** 234 no units (normal 163 to 369)

[redacted] [redacted] **20**[redacted] **RED BLOOD CELLS:** 4.45 no units (normal 4.63 to 6.08)

[redacted] [redacted] **20**[redacted] **RED BLOOD CELLS:** 4.30 no units (normal 4.63 to 6.08)

[redacted] [redacted] **20**[redacted] **RED BLOOD CELLS:** 4.19 no units (normal 4.63 to 6.08)

[redacted] [redacted] **20**[redacted] **WHITE BLOOD CELLS:** 11.77 no units (normal 4.00 to 10.04)

[redacted] [redacted] **20**[redacted] **WHITE BLOOD CELLS:** 7.77 no units (normal 4.00 to 10.04)

[redacted] [redacted] **20**[redacted] **WHITE BLOOD CELLS:** 6.30 no units (normal 4.00 to 10.04)

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
急性心不全	X			
うっ血性心不全	X			
慢性閉塞性肺疾患	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
HEARING DISORDER: CONGENITAL ABSENCE RIGHT EAR	19[redacted]
OTHER: CONGENITAL ABSENCE RIGHT EAR	19
OTHER: PULMONARY EMBOLISM	19
CROHN'S DISEASE	19
OTHER: LOWER BACK PAIN	19
OTHER: ORAL APHTHOUS ULCERS	19
COGNITIVE OR PSYCHIATRIC DISORDER: ANXIETY	19
OSTEOARTHRITIS	19
OTHER: ANXIETY	19
SLEEP APNEA	19
HYPERTENSION	20
ANEMIA: ANEMIA OF CHRONIC DISEASE	20
ANEMIA: UNKNOWN WHAT TYPE	20
CANCER: BASAL CELL CARCINOMA LEFT NOSTRIL	20
DIABETES MELLITUS: DIABETES MELLITUS II	20
DIABETES MELLITUS: TYPE 2	20
GASTROESOPHAGEAL REFLUX DISEASE: WITH ESOPHAGITIS	20
OTHER: BARRETT'S ESOPHAGUS WITHOUT DYSPLASIA	20
OTHER: GASTRITIS WITH GASTRIC EROSIONS	20
OTHER: H. PYLORI NEGATIVE GASTRITIS	20
OTHER: IRREGULAR Z LINE	20
OTHER: IRREGULAR Z-LINE	20
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE: COPD	20
EYE DISEASE/DISORDER: BILATERAL CATARACTS	20
OTHER: CATARACTS BOTH EYES	20
OBESITY	20
OTHER: GATROPARESIS	20
OTHER: UMBILICAL HERNIA	20[redacted]

OTHER: DENTAL CARIES	20[redacted]
OTHER: SHINGLES	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	19[redacted]
SURGERY: TOTAL LEFT KNEE REPLACEMENT	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
SURGERY: COLONOSCOPY	20[redacted]
SURGERY: ESOPHAGOGASTRODUODENOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	10 CIGARETTE	42	
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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 84	[redacted]20[redacted] / 84	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 84	[redacted]20[redacted] / 84	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 118	[redacted]20[redacted] / 118	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 118	[redacted]20[redacted] / 118	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 180	[redacted]20[redacted] / 180	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 180	[redacted]20[redacted] / 180	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 230	[redacted]20[redacted] / 230	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 230	[redacted]20[redacted] / 230	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ALPRAZOLAM	1 mg	PRN	Y-M: 19[redacted]
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]
METFORMIN	2000 mg	QD	Y-M: 20[redacted]
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]
LISINOPRIL	20 mg	QD	Y-M: 20[redacted]
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]
CARVEDILOL	6.25 mg	BID	Y-M: 20[redacted]
CLONIDINE	0.2 mg	QD	Y-M: 20[redacted]
DULOXETINE	20 mg	BID	Y-M: 20[redacted]
METOPROLOL	50 mg	QD	Y-M: 20[redacted]
PIOGLITAZONE	45 mg	QD	Y-M: 20[redacted]
UMECLIDINIUM BROMIDE W/VILANTEROL TRIFENATATE	1 OTHER: PUFF	QD	Y-M: 20[redacted]
MINERALS NOS W/VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted]
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted]

GLIPIZIDE	10 mg	QD	Y-M: 20[redacted]
OXYCOCET	2.5/325 mg	PRN	Y-M: 20[redacted]
VALSARTAN	320 mg	QD	Y-M: 20[redacted]
OLMESARTAN	30 mg	QD	Y-M: 20[redacted] / -95
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 51
OXYCOCET	5/325 mg	PRN	Y-M: 20[redacted] / 51
PREDNISONE	60 mg	QD	Y-M: 20[redacted] / 51
IRON	65 OTHER: MG	QD	Y-M: 20[redacted] / 59

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]	ONGOING
MINERALS NOS W/VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
BENZONATATE	100 mg	TID	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 124
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 125
IPRATROPIUM W/SALBUTAMOL	3 mL	PRN	Y-M: 20[redacted] / 153	Y-M: 20[redacted] / 153
METHYLPREDNISOLONE	.25 mg	OTHER: ONE TIME	Y-M: 20[redacted] / 153	Y-M: 20[redacted] / 153
INSULIN LISPRO	1 OTHER: UNIT	OTHER: Q4H	Y-M: 20[redacted] / 154	ONGOING
OLMESARTAN	40 mg	QD	Y-M: 20[redacted] / 154	ONGOING
OXYCOCET	10-325 mg	PRN	Y-M: 20[redacted] / 154	ONGOING
VICODIN	10-325 kg	PRN	Y-M: 20[redacted] / 154	ONGOING
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 154	Y-M: 20[redacted] / 157
FORMOTEROL	20-2 OTHER: MCG-ML	BID	Y-M: 20[redacted] / 154	Y-M: 20[redacted] / 157
IPRATROPIUM	.5-2.5 OTHER: MG-ML	TID	Y-M: 20[redacted] / 154	Y-M: 20[redacted] / 157
NICOTINE	21 mg	OTHER: 24 HOURS	Y-M: 20[redacted] / 154	Y-M: 20[redacted] / 157
VALSARTAN	160 mg	QD	Y-M: 20[redacted] / 154	Y-M: 20[redacted] / 157
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 155	ONGOING
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / 157	ONGOING

FUROSEMIDE	40 mg	QD	Y-M: 20[redacted] / 157	ONGOING
REGADENOSON	.4-5 OTHER: MG-ML	OTHER: ONE TIME	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 157
METHYLPREDNISOLONE	60 mg	OTHER: ONCE	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 233
MORPHINE	2 mg	PRN	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 234
DICYCLOVERINE	40 mg	QID	Y-M: 20[redacted] / 234	ONGOING
IPRATROPIUM	2 OTHER: PUFFS	PRN	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 234
SODIUM POLYSTYRENE SULFONATE	16 g	OTHER: ONCE	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 234
BUMETANIDE	1 mg	BID	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 235
VALSARTAN	160 mg	QD	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 235
FISH OIL	350 mg	BID	Y-M: 20[redacted] / 235	ONGOING

Event #1: Serious Adverse Event

Event Description	CONGESTIVE HEART FAILURE, COPD EXACERBATION
Preferred Term	うっ血性心不全
AE Onset Date / Rx Day	[redacted]20[redacted] / 153
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 153): NPTST071-BNP: 3100 [0 - 900] PG/ML; NPTST531-TROPONIN: 14 [6 - 14] NG/ML

Microbiology

[redacted]20[redacted] (Rx Day 155): BLOOD GRAM NEGATIVE, GRAM POSITIVE BL: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 153): EKG:NORMAL; [redacted]20[redacted] (Rx Day 155): ECHO-CARDIOGRAM:MILD CONCENTRIC LEFT VENTRICULAR HYPERTROPHY. LEFT VENTRICLE APPEARS HYPERDYNAMIC. THE ESTIMATED EJECTION FRACTION IS >65%. ABNORMAL LEFT VENTRICULAR DIASTOLIC FUNCTION IS OBSERVED. LEFT ATRIUM IS MIL; [redacted]20[redacted] (Rx Day 157): CHEMICAL STRESS TEST:NEGATIVE FOR ISCHEMIA

AE Stopped Rx Day	158
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	COPD EXACERBATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	CONGESTIVE HEART FAILURE, COPD EXACERBATION
Preferred Term	慢性閉塞性肺疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 153
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 153): NPTST071-BNP: 3100 [0 - 900] PG/ML; NPTST531-TROPONIN: 14 [6 - 14] NG/ML

Microbiology

[redacted]20[redacted] (Rx Day 155): BLOOD GRAM NEGATIVE, GRAM POSITIVE BL: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 153): EKG:NORMAL; [redacted]20[redacted] (Rx Day 155): ECHO-CARDIOGRAM:MILD CONCENTRIC LEFT VENTRICULAR HYPERTROPHY. LEFT VENTRICLE APPEARS HYPERDYNAMIC. THE ESTIMATED EJECTION FRACTION IS >65%. ABNORMAL LEFT VENTRICULAR DIASTOLIC FUNCTION IS OBSERVED. LEFT ATRIUM IS MIL; [redacted]20[redacted] (Rx Day 157): CHEMICAL STRESS TEST:NEGATIVE FOR ISCHEMIA

AE Stopped Rx Day	158
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	COPD EXACERBATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	ACUTE CHF EXACERBATION
Preferred Term	急性心不全
AE Onset Date / Rx Day	[redacted]20[redacted] / 233 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 233): Erythrocytes: 4.1 [4.2 - 5.4] 10^12/L; Hemoglobin: 83 [120 - 160] G/L; Leukocytes: 13.4 [4.8 - 10.8] 10^9/L; NPTST071-BNP: 550 [0 - 900] PG/ML; Potassium: 5.7 [3.3 - 4.9] MMOL/L; Sodium: 126 [135 - 145] MMOL/L; [redacted]20[redacted] (Rx Day 234): Erythrocytes: 4 [4.2 - 5.4] 10^12/L; Hemoglobin: 81 [120 - 160] G/L; Leukocytes: 12.9 [4.8 - 10.8] 10^9/L; Potassium: 5 [3.3 - 4.9] MMOL/L; Sodium: 129 [135 - 145] MMOL/L; [redacted]20[redacted] (Rx Day 235): Erythrocytes: 4.2 [4.2 - 5.4] 10^12/L; Hemoglobin: 86 [120 - 160] G/L; Leukocytes: 14.7 [4.8 - 10.8] 10^9/L; Potassium: 4.2 [3.3 - 4.9] MMOL/L; Sodium: 129 [135 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 233): BILATERAL LEG ULTRASOUND DOPPLER:NEGATIVE- TO RULE OUT DVT; CHEST-X-RAY SINGLE VIEW:CARDIOMEGALY WITH MILD PULMONARY VASCULAR CONGESTION

AE Stopped Rx Day	235 (5 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS

Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	HISTORY OF CHF
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

米国の治験責任医師からの報告。本被験者は6[redacted]歳女性であり，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，うっ血性心不全及び COPD 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，不安，変形性関節症，睡眠時無呼吸，高血圧，2 型糖尿病，COPD，肥満，紙巻タバコ喫煙者（1 日 10 本を 42 年間）及び飲酒者（1 日 2 杯未満）であった。

投与 153 日後，被験者はうっ血性心不全及び COPD 増悪を発現した。投与 158 日後，うっ血性心不全及び COPD 増悪は消失した。

本事象発現前（投与 120 日後から投与 126 日後まで），被験者は COPD 増悪（非重篤）を発現していた。

投与 153 日後，被験者は息切れ，間欠性胸痛，下肢浮腫，水分過負荷及び悪寒があったため，入院した。身体的診察，臨床検査，ストレス試験，超音波検査及び心電図検査を実施した。心血管検査で，心拍数は正常でリズムは整，I 音及び II 音は正常で雑音は認められなかった。呼吸器検査で，両側に呼吸音があり，両側に低音性連続性ラ音が認められた。投与 157 日後，慢性心不全の治療計画が策定され，被験者は退院した。

投与された薬剤は，Norco，Percocet，バルサルタン，ソル・メドロール，アトロベント，Perforomist，アセトアミノフェン，メトプロロール，オルメサルタン，フロセミド及びアルブテロール・イプラトロピウム合剤であった。

The patient's past medications include:

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

CLONIDINE HCL for HYPERTENSION (20[redacted] - [redacted] 20[redacted])

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

Causality for RISANKIZUMAB (Blinded)

---

1) Congestive heart failure (10010684) (Cardiac failure congestive (10007559)) [v.22.1] [10010684]

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

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

Dechallenge: Not Applicable

2) COPD exacerbation (10010953) (Chronic obstructive pulmonary disease (10009033)) [v.22.1] [10010953]

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 CONGESTIVE HEART FAILURE , COPD EXACERBATION

- Investigator: COPD EXACERBATION

- AbbVie: Risk factors include pre-existing COPD, diabetes mellitus, and hypertension.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD PRESSURE: 139/58mmHg

[redacted] 20[redacted] BNP (B-TYPE NATRIURETIC PEPTIDE): 3100 PG/ML (normal 0 to 900)

[redacted] 20[redacted] CHEMICAL STRESS TEST: Negative for ischemia

[redacted] **20[redacted] ECHO-CARDIOGRAM:** MILD CONCENTRIC LEFT VENTRICULAR HYPERTROPHY. LEFT VENTRICLE APPEARS HYPERDYNAMIC. THE ESTIMATED EJECTION FRACTION IS >65%. ABNORMAL LEFT VENTRICULAR DIASTOLIC FUNCTION IS OBSERVED. LEFT ATRIUM IS MILDLY DILATED. RIGHT ATRIUM IS MILDLY DILATED. THERE IS TRACE MITRAL REGURGITATION AND MILD TRICUSPID REGURGITATION. RIGHT VENTRICULAR SYSTOLIC PRESSURE IS CALCULATED AT 56MMHG. THERE IS EVIDENCE OF MODERATE PULMONARY HYPERTENSION.

[redacted] 20[redacted] EKG: Normal

[redacted] 20[redacted] GRAM MEGATIVE, GRAM POSITIVE BLOOD CULTURE: Negative

[redacted] **20[redacted] NYHA SCORE:** II - Mild symptoms and slight limitation during ordinary activity

[redacted] 20[redacted] PULSE: 90 bpm

[redacted] 20[redacted] RESPIRATORY RATE: 18 /min

[redacted] 20[redacted] TEMPERATURE: 97.4 F

[redacted] **20[redacted] TROPONIN:** 14 ng/L (normal 6 to 14)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

米国の治験責任医師からの報告。本被験者は 6[redacted] 歳女性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，慢性心不全急性増悪の事象を発現した。

Event 3 の臨床経過：

関連する病歴は，睡眠時無呼吸，高血圧，慢性疾患の貧血，貧血（タイプ不明），2 型糖尿病，慢性閉塞性肺疾患，肺気腫，クローン病，肥満，喫煙者（1 日 10 本を 42 年間）及び飲酒者（1 日 2 杯未満）であった。

投与 233 日後，被験者は慢性心不全急性増悪を発現した。投与 235 日後，慢性心不全急性増悪は消失した。

投与 233 日後，被験者は両側下肢の疼痛及び腫脹があり，来院した。被験者は，利尿剤とフロセミドを自宅で服用していたが，症状は軽快していなかった。発熱，咳嗽及び動悸はなかった。臨床検査の結果，低ナトリウム血症及び高カリウム血症は顕著で，BNP は 500 台，軽度の白血球増加症であった。胸部 X 線検査の結果，慢性心不全増悪と一致する両側性肺血管うっ血が認められた。Bumex の静脈内投与での利尿によってすぐに正常血液量となった。身体的診察で異常は認められなかった。投与 235 日後，被験者は退院し，ラシックスの毎日投与は継続とな

った。退院時，両側性浮腫の痕跡も認められた。

治験責任医師によると，慢性心不全，COPD，肥満，高血圧及び 2 型糖尿病はリスク因子と考えられた。

投与された薬剤は，シプロフロキサシン，オメガ-3，アトロベント，ソル・メドロール，モルヒネ，バルサルタン，Bumex 及びジサイクロミンであった。

The patient's past medications include:

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

CLONIDINE HCL for HYPERTENSION (20[redacted] - [redacted] 20[redacted])

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

Causality for RISANKIZUMAB (Blinded)

---

1) Acute heart failure (10000803) (Cardiac failure acute (10007556)) [v.22.1] [10000803]

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 CHF EXACERBATION

- Investigator: History of CHF

- AbbVie: event is more likely related to pre-existing history of congestive heart failure per PI. Additional risk factors include pre-existing hypertension and diabetes mellitus.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] **20[redacted] BNP:** 550 PG/ML (normal 0 to 900)

[redacted] 20[redacted] **CHEST X-RAY SINGLE VIEW:** Cardiomegally with mild pulmonary vascular congestion

[redacted] 20[redacted] **HEMOGLOBIN:** 8.3 G/DL (normal 12.0 to 16.0)

[redacted] 20[redacted] **HEMOGLOBIN:** 8.1 G/DL (normal 12.0 to 16.0)

[redacted] 20[redacted] **HEMOGLOBIN:** 8.6 G/DL (normal 12.0 to 16.0)

[redacted] 20[redacted] **POTASSIUM:** 5.7 MMOL/L (normal 3.3 to 4.9)

[redacted] 20[redacted] **POTASSIUM:** 5.0 MMOL/L (normal 3.3 to 4.9)

[redacted] 20[redacted] **POTASSIUM:** 4.2 MMOL/L (normal 3.3 to 4.9)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.05 10^6/uL (normal 4.20 to 5.40)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.01 10^6/uL (normal 4.20 to 5.40)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.2 10^6/uL (normal 4.20 to 5.40)

[redacted] 20[redacted] **SODIUM:** 126 MMOL/L (normal 135 to 145)

[redacted] 20[redacted] **SODIUM:** 129 MMOL/L (normal 135 to 145)

[redacted] 20[redacted] **SODIUM:** 129 MMOL/L (normal 135 to 145)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 13.4 10^3/uL (normal 0 to 900)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 12.9 10^3/uL (normal 0 to 900)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 14.7 10^3/uL (normal 0 to 900)

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
痔瘻	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: NA	NOT REPORTED
LATENT TUBERCULOSIS	NOT REPORTED
CROHN'S DISEASE	19[redacted]
INFLAMMATORY BOWEL DISEASE: CROHN'S DISEASE	19[redacted]
INFLAMMATORY BOWEL DISEASE: RESECTION OF TERMINAL ILEUM	20[redacted]
OTHER: SLEEP INSOMNIA	20[redacted]
OTHER: MENOPAUSE	20[redacted]
OTHER: MENSTRUAL PAIN	20[redacted]
OTHER: VITAMIN B12 DEFICIENCY	20[redacted]
OTHER: VITAMIN D DEFICIENCY	20[redacted]
OTHER: BILE ACID MALABSORPTION	20[redacted]
OTHER: PERIANAL FISTULA	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	19[redacted]
SURGERY: HEMICOLECTOMY	19[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	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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 33	[redacted] / 33	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 33	[redacted] / 33	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 54	[redacted] / 54	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 54	[redacted] / 54	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 92	[redacted] / 92	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 148	[redacted] / 148	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 197	[redacted] / 197	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 264	[redacted] / 264	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 313	[redacted] / 313	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 372	[redacted] / 372	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 428	[redacted] / 428	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
NAPROXEN	500 mg	PRN	Y-M: 20[redacted]
ZOPICLONE	3.75 mg	PRN	Y-M: 20[redacted]
BIFIDOBACTERIUM INFANTIS	1 OTHER: TAB	QD	Y-M: 20[redacted]
CYANOCOBALAMIN	1000 ug	OTHER: QMONTHLY	Y-M: 20[redacted]
ERGOCALCIFEROL	3000 OTHER: UNITS	QD	Y-M: 20[redacted]
IRON	2 OTHER: VIALS	OTHER: Q2M PRN	Y-M: 20[redacted]
PANTOPRAZOLE	1 OTHER: TAB	QD	Y-M: 20[redacted]
COLESTIPOL	0.5 mg	OTHER: QHS	Y-M: 20[redacted] / -261
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted] / -29
FENTANYL	100 ug	OTHER: ONCE	Y-M: 20[redacted] / -10
MIDAZOLAM	5 mg	OTHER: ONCE	Y-M: 20[redacted] / -10

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
NAPROXEN	500 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
ZOPICLONE	3.75 mg	PRN	Y-M: 20[redacted]	ONGOING
BIFIDOBACTERIUM INFANTIS	1 OTHER: TAB	QD	Y-M: 20[redacted]	ONGOING
CYANOCOBALAMIN	1000 ug	OTHER: QMONTHLY	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	3000 OTHER: UNITS	QD	Y-M: 20[redacted]	ONGOING
IRON	2 OTHER: VIALS	OTHER: Q2M PRN	Y-M: 20[redacted]	ONGOING
PANTOPRAZOLE	1 OTHER: TAB	QD	Y-M: 20[redacted]	ONGOING
COLESTIPOL	0.5 mg	OTHER: QHS	Y-M: 20[redacted] / 261	ONGOING
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 162	NOT REPORTED
AMITRIPTYLINE	12.5 mg	QD	Y-M: 20[redacted] / 306	NOT REPORTED
CIPROFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 416	Y-M: 20[redacted] / 422
METRONIDAZOLE	500 mg	QD	Y-M: 20[redacted] / 416	Y-M: 20[redacted] / 422
TRAMADOL	100 mg	PRN	Y-M: 20[redacted] / 418	NOT REPORTED
RIFAMPICIN	150 mg	QD	Y-M: 20[redacted] / 537	NOT REPORTED

Event #1: Serious Adverse Event

Event Description	PERI-ANAL FISTULA
Preferred Term	痔瘻
AE Onset Date / Rx Day	[redacted]20[redacted] / 416
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 415): CT ABDOMEN PELVIS W/ CONTRAST:NO NEW FISTULA OR FIBROSTENOSING DISEASE IN THE ABDOMNE/PELIVS. 2.4 CM ABSCESS INT HE LEFT GLUTEAL CLEFT FAT. THIS WOULD BE DRAINABLE VIA TRANSGLUTEAL APPROACH.; [redacted]20[redacted] (Rx Day 417): DRAINAGE, FISTULOTOMY AND SETON PROCEDURE:PATIENT TOLERATED THE PROCEDURE WELL WITH MINIMAL BLOOD LOSS.

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED

Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN'S DISEASE - HISTORY OF PREVIOUS PERIANAL FISTULA
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

カナダの治験責任医師からの報告。本被験者は5[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，肛門周囲瘻の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，貧血，クローン病，腸切除，半結腸切除，回腸末端の切除，回腸末端吻合部の切除，胆汁酸吸収不良，非喫煙者及び飲酒者（1 日 2 杯未満）であった。

投与 416 日後，被験者は肛門周囲瘻を発現した。治験責任医師によると，入院前，被験者は肛門周囲痛（左側）を訴え，抗生物質が投与された。投与 415 日後，被験者は症状の増加を訴え，CT スキャン検査が実施された。投与 416 日後，同部位の不快感が継続するため，被験者は入院した。身体的診察で発熱はなく，肛門左側の位置に硬結が認められた。投与 417 日後，全身麻酔下で手術が実施され，左殿筋の 2 つの大膿瘍のドレナージ及び括約筋貫通痔瘻への 2 つのシートン留置が行われた。投与 418 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，シプロフロキサシン，フラジール及びトラマドールであった。

Causality for RISANKIZUMAB (Blinded)

---

1) Perianal fistula (10068659) (Anal fistula (10002156)) [v.23.1] [10068659]

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 PERI-ANAL FISTULA

- Investigator: Crohns Disease - history of previous perianal fistula

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN PELVIS:** w/ CONTRAST: NO NEW FISTULA OR FIBROSTENOSING DISEASE IN THE ABDOMNE/PELIVS. 2.4 CM ABSCESS INT HE LEFT GLUTEAL CLEFT FAT. THIS WOULD BE DRAINABLE VIA TRANSGLUTEAL APPROACH.

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
基底細胞癌	X			X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Placebo SC Q8W	7[redacted]	MALE	WHITE

Medical History	Onset Year
HYPERLIPIDEMIA: HYPERCHOLESTROL	20[redacted]
OTHER: ARTHRITIS - LOWER BACK	20
OSTEOARTHRITIS: LEFT HIP	20
CROHN'S DISEASE	20
OTHER: ARTHRITIS - RIGHT AND LEFT THUMB	20
OTHER: ARTHRITIS - RIGHT AND LEFT WRIST	20
OTHER: ACID REFLUX - MILD	20
OTHER: HEAVY SUN EXPOSURE	20
OTHER: HEMORRHOIDS	20

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	19[redacted]
SURGERY: LEFT THUMB REPAIR	19
SURGERY: RIGHT KNEE MENISCUS REPAIR	19
SURGERY: RIGHT WRIST BROKEN & REPAIRED	19
SURGERY: LEFT KNEE MENISCUS REPAIR	19
SURGERY: LEFT INGUINAL HERNIA REPAIR	20
SURGERY: RIGHT INGUINAL HERNIA REPAIR	20
SURGERY: LEFT HIP REPLACEMENT	20
CROHN'S DISEASE HISTORY: COLONOSCOPY	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	FORMER			
CIGARETTES	FORMER	3 CIGARETTE	5	19[redacted]
CIGARS	FORMER			
E-CIGARETTES	NEVER			
PIPES	FORMER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 29	[redacted] / 29	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 64	[redacted] / 64	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 88	[redacted] / 88	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 138	[redacted] / 138	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 195	[redacted] / 195	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 256	[redacted] / 256	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 312	[redacted] / 312	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 362	[redacted] / 362	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 431	[redacted] / 431	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ROSUVASTATIN	10 mg	QD	Y-M: [redacted]
MESALAZINE	2 g	BID	Y-M: [redacted]
PARACETAMOL	1 OTHER: PILL	PRN	Y-M: [redacted]
ACETYLSALICYLIC ACID	81 mg	OTHER: EVERY WEEK	Y-M: [redacted]
CALCIUM	650 mg	QD	Y-M: [redacted]
COLECALCIFEROL	400 IU	QD	Y-M: [redacted]
FLEX-A-MIN	1000 mg	QD	Y-M: [redacted]
IRON	1 OTHER: PILL	QD	Y-M: [redacted]
LINUM USITATISSIMUM	1300 mg	QD	Y-M: [redacted]
PANAX QUINQUEFOLIUS	1 OTHER: PILL	QD	Y-M: [redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
ROSUVASTATIN	10 mg	QD	Y-M: [redacted]	NOT REPORTED
PARACETAMOL	1 OTHER: PILL	PRN	Y-M: [redacted]	NOT REPORTED

ACETYLSALICYLIC ACID	81 mg	OTHER: EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
CALCIUM	650 mg	QD	Y-M: 20[redacted]	NOT REPORTED
COLECALCIFEROL	400 IU	QD	Y-M: 20[redacted]	NOT REPORTED
FLEX-A-MIN	1000 mg	QD	Y-M: 20[redacted]	NOT REPORTED
IRON	1 OTHER: PILL	QD	Y-M: 20[redacted]	NOT REPORTED
LINUM USITATISSIMUM	1300 mg	QD	Y-M: 20[redacted]	NOT REPORTED
PANAX QUINQUEFOLIUS	1 OTHER: PILL	QD	Y-M: 20[redacted]	NOT REPORTED
COLYTE	4 L	OTHER: ONCE	Y-M: 20[redacted] / 452	Y-M: 20[redacted] / 453
LIDOCAINE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
PROPOFOL	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453

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

Event Description	BASAL CELL CARCINOMA TO RIGHT TEMPLE OF HEAD
Preferred Term	基底細胞癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 447 (16 DAYS AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 447): BIOPSY:BASAL CELL CARCINOMA, SUPERFICIAL TYPE, EXTENDS TO TISSUE EDGES; [redacted]20[redacted] (Rx Day 585): BASAL CELL CARCINOMA REMOVAL:RE-EXCISION SPECIMEN SHOWING RESIDUAL MICROFOCAL SUPERICIAL MULTICENTRIC BASAL CELL CARCINOMA AND DERMAL FIBROSIS, EXCISED

AE Stopped Rx Day	585 (154 DAYS AFTER LAST TREATMENT)
Duration of AE	139 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SUN EXPOSURE, AGE
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7[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬及びリサンキズマブが投与され，右側頭の基底細胞癌の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元紙巻タバコ喫煙者（1 日 3 本を 5 年間），クローン病，元パイプ喫煙者，元葉巻喫煙者，元噛みタバコ使用者及びアルコール摂取（1 日 2 杯未満）であった。

被験者は，20[redacted]年[redacted]月[redacted]日から 20[redacted]年[redacted]月[redacted]日までのサブスタディ 1 で盲検化された被疑薬に無作為化された。20[redacted]年[redacted]月[redacted]日，非盲検化されたリサンキズマブの投与が開始された。

投与 447 日後，被験者は右側頭に基底細胞癌を発現した。投与 585 日後，右側頭の基底細胞癌は消失した。

かかりつけ医による定期健診で，右側頭にほくろのような領域が認められたが，他の症状はなかった。生検で基底細胞癌が明らかになった。投与 585 日後，基底細胞癌の完全切除が実施された。

治験責任医師によると，リスク因子には，気候が温暖な地域への旅行中の日光への曝露などがあった。

Causality for RISANKIZUMAB (Blinded)

---

1) Basal cell carcinoma (10004146) (Basal cell carcinoma (10004146)) [v.23.1] [10004146]

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) Basal cell carcinoma (10004146) (Basal cell carcinoma (10004146)) [v.23.1] [10004146]

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 BASAL CELL CARCINOMA TO RIGHT TEMPLE OF HEAD

- Investigator: Sun exposure, age.

- AbbVie: Basal cell carcinoma is the most common form of skin cancer and the most frequently occurring form of all cancers. Additional risk factors include advanced age and caucasian race.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of BASAL CELL CARCINOMA TO RIGHT TEMPLE OF HEAD

- Investigator: Sun exposure, age.

- AbbVie: Basal cell carcinoma is the most common form of skin cancer and the most frequently occurring form of all cancers. Additional risk factors include advanced age and caucasian race.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BIOPSY:** Basal Cell carcinoma, superficial type, extends to tissue edges.

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

[redacted] **20[redacted] PATHOLOGY:** Re-excision specimen showing residual microfocal superficial multicentric basal cell carcinoma and dermal fibrosis.

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
脳梗塞	X			X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Placebo SC Q8W	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: MORPHINE	19[redacted]
OTHER: C-SECTION	19
OTHER: C-SECTION	19
OTHER: C-SECTION	19
OTHER: UTERINE BLEEDING	19
INFLAMMATORY BOWEL DISEASE: BOWEL OBSTRUCTION	19
CROHN'S DISEASE	19
OSTEOARTHRITIS: 2ND & 4TH SPINAL VERTEBRAE	19
EYE DISEASE/DISORDER: GLAUCOMA	20
HYPOTHYROIDISM	20
OTHER: JOINT PAIN - KNEE'S & ELBOW	20
OTHER: HEMORRHOIDS	20

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

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	12 CIGARETTE	50	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 31	[redacted]20[redacted] / 31	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 82	[redacted]20[redacted] / 82	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 82	[redacted]20[redacted] / 82	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 115	[redacted]20[redacted] / 115	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 136	[redacted]20[redacted] / 136	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 136	[redacted]20[redacted] / 136	1
PLACEBO		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
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 284	[redacted]20[redacted] / 284	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 338	[redacted]20[redacted] / 338	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 393	[redacted]20[redacted] / 393	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 451	[redacted]20[redacted] / 451	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 508	[redacted]20[redacted] / 508	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
CALCIUM	600 mg	BID	Y-M: 19[redacted]
FISH OIL	2400 mg	QD	Y-M: 19[redacted]
MULTIVITAMIN	1 OTHER: TAB	BID	Y-M: 19[redacted]
CYANOCOBALAMIN	1 OTHER: PILL	QD	Y-M: 19[redacted]
LEVOTHYROXINE	250 mg	QD	Y-M: 19[redacted]
PARACETAMOL	1-2 OTHER: PILL	PRN	Y-M: 19[redacted]
TIMOLOL	1 gtt	BID	Y-M: 20[redacted]
POTASSIUM	600 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
TINZAPARIN	4500 OTHER: UNITS	QD	Y-M: 20[redacted] / 420	Y-M: 20[redacted] / 445
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 421	NOT REPORTED
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / 421	NOT REPORTED
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted] / 421	NOT REPORTED
LEVOTHYROXINE	200 OTHER: MCG	QD	Y-M: 20[redacted] / 421	NOT REPORTED
MACROGOL 3350	17 g	QD	Y-M: 20[redacted] / 421	NOT REPORTED
METFORMIN	500 mg	BID	Y-M: 20[redacted] / 421	NOT REPORTED
PERINDOPRIL	8 mg	QD	Y-M: 20[redacted] / 421	NOT REPORTED
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 421	Y-M: 20[redacted] / 421
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 421	Y-M: 20[redacted] / 674
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 424	Y-M: 20[redacted] / 445
ACETYLSALICYLIC ACID	650 mg	OTHER: ONCE	Y-M: 20[redacted] / 430	Y-M: 20[redacted] / 430

Event #1: Serious Adverse Event, Event of Interest - Adjudicated MACE Event, Event of Interest - Adjudicated Extended MACE Event

Event Description RIGHT MIDDLE CEREBRAL ARTERY TERRITORY INFARCT

Preferred Term 脳梗塞

AE Onset Date / Rx Day [redacted]20[redacted] / 420

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 420): Calcium: 1.32 [1.09 - 1.25] MMOL/L; Calcium: 1.3 [1.09 - 1.25] MMOL/L; Glucose: 8.7 [3.3 - 11] MMOL/L; Hematocrit: 0 [0 - 0] FRACTION OF 1; Hemoglobin: 136 [120 - 160] G/L; NPTST002-02 SATURATION: 80 [50 - 80] %; NPTST028-ANION GAP: 9 [4 - 16] MMOL/L; NPTST050-BAROMETRIC PRESSURE: 706 [NOT REPORTED - NOT REPORTED] MMHG; NPTST051-BASE EXCESS: 1 [-4 - 1] MMOL/L; NPTST107-CARBOXYHEMOGLOBIN: 1.2 [0 - 3] %; NPTST112-CHLORIDE: 107 [98 - 112] MMOL/L; NPTST267-HCO3: 25 [20 - 27] MMOL/L; NPTST315-LACTATE: 1.6 [0.5 - 2.2] MMOL/L; NPTST342-METHEMOGLOBIN: 1.7 [0 - 1.5] %; NPTST393-OXYHEMOGLOBIN: 77 [50 - 80] %; NPTST402-PCO2: 45 [35 - 50] MMHG; NPTST431-PO2: 47 [30 - 50] MMHG; Potassium: 4.2 [3.5 - 5] MMOL/L; Sodium: 141 [135 - 145] MMOL/L; pH: 7.37 [7.3 - 7.4] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 420): ABDOMINAL ANGIOGRAM 1 VESSEL:SUCCESSFUL ENDOVASCULAR THROMBECTOMY WITH RECANALIZATION OF A RIGHT-SIDED M1 OCCLUSION. A PERSISTENT DISTAL POSTERIOR MCA BRANCH OCCLUSION WAS NOTED AS WELL AS SEVERAL NONOCCLUSIVE FILLING DEFECT WITH; CT HEAD:THERE IS A PARTIAL RIGHT MCA TERRITORY INFARCT SEEN ON CT HEAD, PREDOMINANTLY INVOLVING THE INSULAR CORTEX. NO ACUTE HEMORRHAGE. SCATTERED ATHEROMATOUS CHANGES AS DESCRIBED. COMPLETE OCCLUSION OF THE; EXTRACRANIAL STENT PLACEMENT WITH ANGIOPLASTY:SUCCESSFUL ENDOVASCULAR THROMBECTOMY WITH RECANALIZATION OF A RIGHT-SIDED M1 OCCLUSION. A PERSISTENT DISTAL POSTERIOR MCA BRANCH OCCLUSION WAS NOTED AS WELL AS SEVERAL NONOCCLUSIVE FILLING DEFECT WITH; MR BRAIN:EVIDENCE OF RIGHT MCA TERRITORY INFARCT AS DESCRIBED ABOVE. SCATTERED SUBARACHNOID HEMORRHAGE THROUGHOUT THE RIGHT CEREBRAL CONVEXITY SULCI.; NEURO ANGIOGRAM 4 VESSELS:SUCCESSFUL ENDOVASCULAR THROMBECTOMY WITH RECANALIZATION OF A RIGHT-SIDED M1 OCCLUSION. A PERSISTENT DISTAL POSTERIOR MCA BRANCH OCCLUSION WAS NOTED AS WELL AS SEVERAL NONOCCLUSIVE FILLING DEFECT WITH; [redacted]20[redacted] (Rx Day 421): CT HEAD:RECENT RIGHT MCA TERRITORY INFARCT AS SEEN ON MRI EARLIER TODAY AND CT YESTERDAY. MILD SUBARACHNOID BLOOD PRODUCTS OR CONTRAST EXTRAVASATION FROM THE RECENT ENDOVASCULAR PROCEDURE.; [redacted]20[redacted] (Rx Day 422): TRANSTHORACIC ECHOCARDIOGRAM:NORMAL LV SIZE AND SYSTOLIC FUNCTION WITH LV EJECTION FRACTION VISUALLY 55-60%. THERE IS BORDERLINE HYPOKINESIS OF THE SEPTUM. NORMAL RV SIZE AND SYSTOLIC FUNCTION. NO SIGNIFICANT VALVE DISEASE. MODER; VIDEO FLUOROSCOPY SWALLOWING STUDY:NO SWALLOWING ANATOMICAL ABNORMALITY IS IDENTIFIED. A MILD DEGREE OF DEGENERATIVE CHANGE IS NOTED WITHIN THE LOWER CERVICLE SPINE. THE PATIENT HAS HAD PRIOR ANGIOPLASTY AND STENTING FOR A HIGH-GRADE R

AE Stopped Rx Day	445
Duration of AE	26 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ATHEROSCLEROTIC DISEASE RESULTING IN CORONARY ARTERY STENOSIS CAUSING MCA STROKE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	LIFE THREATENING

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，右中大脳動脈領域梗塞の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，甲状腺機能低下症，喫煙者（1 日 12 本を 45 年間）及び非飲酒者であった。

投与 420 日後，被験者は右中大脳動脈領域梗塞を発現した。投与 445 日後，右中大脳動脈領域梗塞は消失した。

投与 420 日後の 5 時 30 分，被験者は目を覚まし，体の左側が「動かない」ように感じた。同日，被験者は顔面麻痺，不明瞭発語，錯乱，左上下肢の使用困難及び左半身の脱力があったため，救急治療室を受診した。被験者は喫煙者とのことであった。診断が行われ，被験者は冠動脈狭窄によって引き起こされた中大脳動脈性卒中と診断された。頭蓋外ステント留置，血管形成，血栓除去及び頸動脈ステント留置が行われた。リハビリテーションのため，入院が継続された。投与 445 日後，被験者は退院した。

治験責任医師によると，被験者の状態は「症候はあっても明らかな障害はない：日常の勤めや活動は行える」であった。

投与された薬剤は，ASA，クロピドグレル及び tinzaparin であった。

The patient's past medications include:

MORPHINE for UNKNOWN INDICATION

Causality for RISANKIZUMAB (Blinded)

---

1) Middle cerebral artery infarct (10027578) (Cerebral infarction (10008118)) [v.23.0] [10027578]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of RIGHT MIDDLE CEREBRAL ARTERY TERRITORY INFARCT

- Investigator: Atherosclerotic disease resulting in coronary artery stenosis causing MCA stroke

- AbbVie: Risk factors include long term and current smoking history of 12 cigarettes per day for 45 years and pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ANGIOGRAM 1 VESSEL:** SUCCESSFUL ENDOVASCULAR THROMBECTOMY WITH RECANALIZATION OF A RIGHT-SIDED M1 OCCLUSION. A PERSISTENT DISTAL POSTERIOR MCA BRANCH OCCLUSION WAS NOTED AS WELL AS SEVERAL NONOCCLUSIVE FILLING DEFECT WITHIN THE RIGHT DISTAL ACA. A RESIDUAL HIGH-GRADE STENOSIS OF THE RIGHT INTERNAL CAROTID ARTERY WAS NOTED, WHICH WAS FURTHER TREATED WITH ANGIOPLASTY AND STENTING SUCCESSFULLY.

[redacted] **20[redacted] BASE EXCESS:** 1 MMOL/L (normal -4 to 1)

[redacted] **20[redacted] CALCIUM:** 1.32 MMOL/L (normal 1.09 to 1.25)

[redacted] **20[redacted] CALCIUM:** 1.30 MMOL/L (normal 1.09 to 1.25)

[redacted] **20[redacted] CT HEAD:** There is a partial right MCA territory infarct seen on CT Head, predominantly involving the insular cortex. No acute hemorrhage. Scattered atheromatous changes as described. Complete occlusion of the cervical right internal carotid artery with absent contrast opacification. Reconstitution of intracranial right ICA, likely from collateral supply. Occluded mid-distal right M1 segment and with involvement of its superior division. CT perfusion suggest partial right MCA territory core infarct with a large ischemic penumbra.

[redacted] **20[redacted] CT HEAD:** Recent right MCA territory infarct as seen on MRI earlier today and CT yesterday. Mild subarachnoid blood products or contrast extravasation from the recent endovascular procedure.

[redacted] **20[redacted] METHEMOGLOBIN:** 1.7 % (normal 0 to 1.5)

[redacted] **20[redacted] MR BRAIN:** Evidence of right MCA territory infarct as described above. Scattered subarachnoid hemorrhage throughout the right cerebral convexity sulci.

[redacted] **20[redacted] NEURO ANGIOGRAM 4 VESSELS:** Successful endovascular thrombectomy with recanalization of a right-sided M1 occlusion. A persistent distal posterior MCA branch occlusion was noted as well as several nonocclusive filling defect within the right distal ACA. A residual high-grade stenosis of the right internal carotid artery was noted, which was further treated with angioplasty and stenting successfully.

[redacted] **20[redacted] O2 SAT:** 80 % (normal 50 to 80)

[redacted] **20[redacted] OXYHEMOGLOBIN:** 77 % (normal 50 to 80)

[redacted] **20[redacted] PCO2:** 45 mmHg (normal 35 to 50)

[redacted] **20[redacted] PH:** 7.37 no units (normal 7.3 to 7.4)

[redacted] 20[redacted] **TRANSTHORACIC ECHOCARDIOGRAM:** Normal LV size and systolic function with LV ejection fraction visually 55-60%. There is borderline hypokinesis of the septum. Normal RV size and systolic function. No significant valve disease. Moderate left atrial enlargement. No obvious cardiac source of embolism identified on this study. Most likely etiology of stroke given clinical history is that of carotid artery stenosis.

[redacted] 20[redacted] **VIDEO FLUOROSCOPY SWALLOWING STUDY:** No swallowing anatomical abnormality is identified. A mild degree of degenerative change is noted within the lower cervicle spine. The patient has had prior angioplasty and stenting for a high-grade right internal carotid artery stenosis.

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			
脂肪肝				X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
EYE DISEASE/DISORDER: FAR-SIGHTED	19[redacted]
OTHER: ICHTHYOSIS	19
OTHER: JOINT PAIN	20
OTHER: LEG ACHES (NIGHTTIME)	20
HYPERTENSION	20
OTHER: HIGH CHOLESTEROL	20
CROHN'S DISEASE	20
DIABETES MELLITUS: TYPE 2 INSULIN DEPENDENT	20
OTHER: YEAST INFECTION (INTERMITTENT)	20

Prior Procedures	Procedure Year
SURGERY: TUBAL LIGATION	19[redacted]
SURGERY: RHINOPLASTY	19
SURGERY: APPENDECTOMY	19
SURGERY: OOPHORECTOMY	19
SURGERY: COMPLETE HYSTERECTOMY	19
CROHN'S DISEASE HISTORY: COLONOSCOPY	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	12 CIGARETTE	41	
CIGARS	NEVER			
E-CIGARETTES	FORMER	4 SESSIONS	1	20[redacted]
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 22	[redacted] / 22	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 56	[redacted] / 56	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 83	[redacted] / 83	1
M16006 /RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 83	[redacted] / 83	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 111	[redacted] / 111	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 154	[redacted] / 154	1
M16006 /RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 154	[redacted] / 154	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 168	[redacted] / 168	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 228	[redacted] / 228	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 273	[redacted] / 273	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 343	[redacted] / 343	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 399	[redacted] / 399	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 447	[redacted] / 447	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 497	[redacted] / 497	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
LIRAGLUTIDE	2.4 mg	QD	Y-M: 20[redacted]
OTHER LIPID MODIFYING AGENTS	20 mg	QD	Y-M: 20[redacted]
INSULIN GLARGINE	16 OTHER: UNITS	QD	Y-M: 20[redacted]
LOSARTAN	50 mg	QD	Y-M: 20[redacted]
INSULIN LISPRO	8 - 11 OTHER: UNITS	TID	Y-M: 20[redacted]
PIMECROLIMUS	N/A (1%) %	BID	Y-M: 20[redacted] / 49
XAMIOL	N/A (50-.05%) %	QD	Y-M: 20[redacted] / 49

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
NUROFEN COLD AND FLU	2 OTHER: TABS	PRN	Y-M: 20[redacted] / 216	NOT REPORTED
LOSARTAN	50 mg	QD	Y-M: 20[redacted] / 313	NOT REPORTED
SERRAPEPTASE	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / 404	Y-M: 20[redacted] / 434
PARACETAMOL	500 mg	OTHER: Q4-6 HRS, PRN	Y-M: 20[redacted] / 454	NOT REPORTED
COLYTE	4 L	OTHER: ONCE	Y-M: 20[redacted] / 525	Y-M: 20[redacted] / 526
PROPOFOL	150 mg	OTHER: ONCE	Y-M: 20[redacted] / 526	Y-M: 20[redacted] / 526
BACLOFEN	20 mg	TID	Y-M: 20[redacted] / 538	NOT REPORTED
MORPHINE	5 mg	PRN	Y-M: 20[redacted] / 586	Y-M: 20[redacted] / 589
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / 590	NOT REPORTED
ULTRACET	2 OTHER: TABS	PRN	Y-M: 20[redacted] / 590	NOT REPORTED
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 590	Y-M: 20[redacted] / 590
ECHINACEA PURPUREA	1200 mg	QD	Y-M: 20[redacted] / 616	NOT REPORTED
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 638	NOT REPORTED
RANITIDINE	150 mg	PRN	Y-M: 20[redacted] / 708	NOT REPORTED
INSULIN DEGLUDEC	36 OTHER: UNITS	QD	Y-M: 20[redacted] / 714	NOT REPORTED
ACTIDUE	1 OTHER: DOSE	PRN	Y-M: 20[redacted] / 762	NOT REPORTED

Event #1: Event of Interest - Hepatic Events

Event Description FATTY LIVER DISEASE
Preferred Term 脂肪肝
AE Onset Date / Rx Day [redacted]20[redacted] / 364
Age at AE Onset 5[redacted]
Laboratory Testing
NOT APPLICABLE
Microbiology
NOT APPLICABLE

SAE Supplemental Procedure
NOT APPLICABLE

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

Event #2: Serious Adverse Event

Event Description	ABDOMINAL PAIN
Preferred Term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 448
Age at AE Onset	5[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 586): Leukocytes: 11.2 [4 - 11] 10^9/L; Neutrophils: 7.7 [1.8 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 587): C Reactive Protein: 13 [0 - 10] MG/L; [redacted]20[redacted] (Rx Day 588): C Reactive Protein: 18 [0 - 10] MG/L; [redacted]20[redacted] (Rx Day 589): C Reactive Protein: 15 [0 - 10] MG/L; Leukocytes: 13.8 [4 - 11] 10^9/L; Neutrophils: 11.2 [1.8 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 590): C Reactive Protein: 14 [0 - 10] MG/L; Leukocytes: 13.4 [4 - 11] 10^9/L; Neutrophils: 8.2 [1.8 - 7.5] 10^9/L

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 534): MR ABDOMEN:NO STONES IN GALLBLADDER. NO GALLBLADDER WALL TCKENING OR PERICHOLECYSTIC EDEMA. THE INTRA AND EXTRAHEPATIC BILE DUCTS ARE NORMAL IN CALIBER AND CONTOUR WITH NO EVIDENCE OF CHOLEDOCHOLITHIASIS SENT; [redacted]20[redacted] (Rx Day 586): XRAY- ABD SERIES, 2 VIEW AND CHEST:LUNGS ARE CLEAR AND NO INTRATHORACIC PATHOLOGY IS APPARENT. BOWEL GAS PATTERN IS NORMAL. NO APPRECIABLE SOFT TISSUE CALCIFICATION. MILD DEGENERATIVE CHANGES ARE NOTED AT BOTH HIP JOINTS; [redacted]20[redacted] (Rx Day 587): CT ABDOMEN + PELVIS AUGMENTED:1. LOOPS OF LARGE AND SMALL BOWEL ARE UNREMARKABLE WITH NO DIVERTICULOSIS. NO ABNORMAL BOWEL WALL THICKENING OR ABNORMAL MUCOSAL ENHANCEMENT. 2. NO ACUTE INTRA-ABDOMINAL ABNORMALITIES ARE DEMONSTRAT

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	STEROID USE
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

カナダの治験責任医師からの報告。本被験者は5[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，腹痛の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，卵管結紮，虫垂切除，卵巣摘除，完全子宮摘出，元電子タバコ使用者（1 日 4 回を 1 年間），コレステロール高値，高血圧，クローン病，2 型糖尿病（インスリン依存状態），喫煙者（1 日 12 本を 41 年間）及び飲酒者（1 日 2 杯未満）であった。

被験者はサブスタディ 1 に組み入れられていた。

投与 448 日後，被験者は腹痛を発現した。

投与から約 15 ヵ月後以降，腹痛が継続した。MRI が実施され，結果は正常であった。

投与 586 日後，被験者は腹痛が続くため来院し，同日，入院した。被験者によると，膿瘍の可能性があると言われたが，最終診断はなかったとのことであった。医師は，ステロイド治療に続発した腹痛を疑った。入院中，CT スキャン検査が実施された。手術は計画されず，合併症はなかった。入院中，抗生物質による治療が 1 コース行われた。投与 590 日後，被験者は退院し，疼痛についてはステロイド，パントプラゾール及び Tramacet の投与となった。

治験責任医師によると，被験者にはクローン病，脂肪性肝疾患（非重篤）及び憩室炎の既往のリスク因子があった。

投与された薬剤は，モルヒネ，ロセフィン，フラジール，Tramacet，パントプラゾール及び Maxeran であった。

Causality for RISANKIZUMAB (Blinded)

---

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

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 ABDOMINAL PAIN

- Investigator: Steroid use

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN + PELVIS AUGMENTED:** 1. Loops of large and small bowel are unremarkable with no diverticulosis. No abnormal bowel wall thickening or abnormal mucosal enhancement. 2. No acute intra-abdominal abnormalities are demonstrated

[redacted] **20[redacted] MR ABDOMEN:** No stones in gallbladder. No gallbladder wall tckening or pericholecystic edema. The intra and extrahepatic bile ducts are normal in caliber and contour with no evidence of choledocholithiasis

20[redacted] MRCP: Mild fatty liver (non serious) and otherwise normal

[redacted] 20[redacted] MRI: Normal

[redacted] **20[redacted] XRAY- ABD SERIES, 2 VIEW AND CHEST:** Lungs are clear and no intrathoracic pathology is apparent. Bowel gas pattern is normal. No appreciable soft tissue calcification. Mild degenerative changes are noted at both hip joints

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
急性腎障害	X			
脂肪肝				X
肺炎	X			X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: ABDOMINAL PAIN	19[redacted]
OTHER: DIARRHEA	19
CROHN'S DISEASE	19
OTHER: VITAMIN B 12 DEFICIENCY	20
HEARING DISORDER: MENIER'S SYNDROME	20
OTHER: JOINT PAIN	20
DEPRESSION: DEPRESSION	20
HYPERTENSION	20
OTHER: HIGH CHOLESTEROL	20
ANEMIA: LOW IRON	20
OTHER: BLADDER RETENTION	20
OTHER: KIDNEY STONES	20

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

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	20 CIGARETTE	15	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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 23	[redacted]20[redacted] / 23	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 23	[redacted]20[redacted] / 23	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 53	[redacted]20[redacted] / 53	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 53	[redacted]20[redacted] / 53	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 86	[redacted]20[redacted] / 86	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 86	[redacted]20[redacted] / 86	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 114	[redacted]20[redacted] / 114	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 142	[redacted]20[redacted] / 142	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 142	[redacted]20[redacted] / 142	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 173	[redacted]20[redacted] / 173	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 173	[redacted]20[redacted] / 173	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 226	[redacted]20[redacted] / 226	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 226	[redacted]20[redacted] / 226	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 288	[redacted]20[redacted] / 288	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 288	[redacted]20[redacted] / 288	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 346	[redacted]20[redacted] / 346	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 346	[redacted]20[redacted] / 346	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 404	[redacted]20[redacted] / 404	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 404	[redacted]20[redacted] / 404	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 451	[redacted]20[redacted] / 451	1

RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 451	[redacted]20[redacted] / 451	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 506	[redacted]20[redacted] / 506	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 506	[redacted]20[redacted] / 506	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
CYANOCOBALAMIN	1 mL	OTHER: MONTHLY	Y-M: 20[redacted]
VITAMIN B COMPLEX	1 OTHER: TAB	QD	Y-M: 20[redacted]
CALCIUM	650 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	2 OTHER: TABS	QD	Y-M: 20[redacted]
GINKGO BILOBA	60 mg	QD	Y-M: 20[redacted]
LECITHIN	1200 mg	QD	Y-M: 20[redacted]
PROBIOTICS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
SALMON OIL	300 mg	QD	Y-M: 20[redacted]
VITAMINS NOS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
GLUCOSAMINE	500/400 mg	QD	Y-M: 20[redacted]
ARIPIPRAZOLE	2.5 mg	QD	Y-M: 20[redacted]
ROSUVASTATIN	10 mg	QD	Y-M: 20[redacted]
IRON	300 mg	OTHER: ONCE EVERY 3 DAYS	Y-M: 20[redacted] / -87
CITALOPRAM	20 mg	QD	Y-M: 20[redacted] / -58
LOSARTAN	50 mg	QD	Y-M: 20[redacted] / -37
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / -37
COLESTYRAMINE	4 g	BID	Y-M: 20[redacted] / 142
BETAHISTINE	8 mg	QD	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
BETAHISTINE	8 mg	QD	Y-M: 20[redacted] / 166	NOT REPORTED
TELMISARTAN	40 mg	QD	Y-M: 20[redacted] / 527	NOT REPORTED
PICO-SALAX	3 OTHER: SACHETS	OTHER: ONCE	Y-M: 20[redacted] / 539	Y-M: 20[redacted] / 540
FENTANYL	75 mg	OTHER: ONCE	Y-M: 20[redacted] / 540	Y-M: 20[redacted] / 540

Event #1: Serious Adverse Event

Event Description	MILD ACUTE KIDNEY INJURY
Preferred Term	急性腎障害

AE Onset Date / Rx Day	[redacted]20[redacted] / 522 (16 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 522): NPTST152-COVID-19 TESTING- NUCLEIC ACID: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; [redacted]20[redacted] (Rx Day 524): NPTST145-COVID 19 TESTING-NUCLEIC ACID: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 521): ECG:SINUS RHYTHM. LOW VOLTAGE, PRECORDIAL LEADS. BORDERLINE T ABNORMALITIES, INFERIOR LEADS; [redacted]20[redacted] (Rx Day 522): CT CHEST FOR PULMONARY EMBOLUS, ENHANCED:NO EVIDENCE OF PULMONARY EMBOLISM. REDUCED LUNG VOLUME WITH EXTENSIVE PATCHY PULMONARY OPACITIES FAVORED TO BE LARGELY RELATED TO ATELECTASIS. SUPERIMPOSED INFECTION OR EDEMA IS NOW EXCLUDED. SMALL BI; ECG:SINUS RHYTHM. ENTRUCULAR PREMATURE COMPLEX. PROBABLE LEFT VENTRICULAR HYPERTROPHY. BORDERLINE T ABNORMALITIES, INFERIOR LEADS; ECG:SINUS RHYTHM. PROBABLE LEFT ATRIAL ENLARGEMENT. LOW VOLTAGE, PRECORDIAL LEADS. PROBABLE LVH WITH SECONDARY REPOL ABNRM; GR CHEST 2 PROJECTIONS:SUBOPTIMAL INSPIRATION. NO OBVIOUS ACUTE ABNORMALITY.; US ABDOMEN, COMPLETE:UNCOMPLICATED CHOLELITHIASIS. PROBABLE HEPATIC STEATOSIS. OTHERWISE UNREMARKABLE EXAMINATION. SOME TECHNICAL LIMITATION NOTED.; [redacted]20[redacted] (Rx Day 523): ABDOMEN, 2 OR MORE PROECTIONS:PATCHY INTERSTITIAL AND AIRSPACE OPACITIES IN BOTH LUNGS WERE DESCRIBED IN THE PREVIOUS CT SCAN IS MOST LIKELY REPRESENTING ATELECTASIS HOWEVER SUPERIMPOSED INFECTION CANNOT BE EXCLUDED I SUGGEST CLIN; CHEST SUPINE AP:PATCHY INTERSTITIAL AND AIRSPACE OPACITIES IN BOTH LUNGS WERE DESCRIBED IN THE PREVIOUS CT SCAN IS MOST LIKELY REPRESENTING ATELECTASIS HOWEVER SUPERIMPOSED INFECTION CANNOT BE EXCLUDED 1 SUGGEST CLIN; ECG:SINUS RHYTHM. VENTRICULAR PREMATURE COMPLEX. LOW VOLTAGE, PRECORDIAL LEADS. BORDERLINE T ABNORMALITIES, INFERIOR LEADS; [redacted]20[redacted] (Rx Day 526): US ABDOMEN, COMPLETE 2 OR MORE ORGANS:CHOLELITHIASIS AND GALLBLADDER SLUDGE WITH NO FEATURES OF ACUTE CHOLECYSTITIS. LIMITED VISUALIZATION OF TEH CBD WITH NORMAL CALIBER MEASURED AT 3MM. NO INTRAHEPATIC BILIARY DILATATION. MODERATE FATTY

AE Stopped Rx Day	526 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	LIKELY DUE TO MEDICATIONS GIVEN IN HOSPITAL
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	COMMUNITY ACQUIRED PNEUMONIA
Preferred Term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 522 (16 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 522): NPTST152-COVID-19 TESTING- NUCLEIC ACID: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; [redacted]20[redacted] (Rx Day 524): NPTST145-COVID 19 TESTING-NUCLEIC ACID: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 521): ECG:SINUS RHYTHM. LOW VOLTAGE, PRECORDIAL LEADS. BORDERLINE T ABNORMALITIES, INFERIOR LEADS; [redacted]20[redacted] (Rx Day 522): CT CHEST FOR PULMONARY EMBOLUS, ENHANCED:NO EVIDENCE OF PULMONARY EMBOLISM. REDUCED LUNG VOLUME WITH EXTENSIVE PATCHY PULMONARY OPACITIES FAVORED TO BE LARGELY RELATED TO ATELECTASIS. SUPERIMPOSED INFECTION OR EDEMA IS NOW EXCLUDED. SMALL BI; ECG:SINUS RHYTHM. ENTRUCULAR PREMATURE COMPLEX. PROBABLE LEFT VENTRICULAR HYPERTROPHY. BORDERLINE T ABNORMALITIES, INFERIOR LEADS; ECG:SINUS RHYTHM. PROBABLE LEFT ATRIAL ENLARGEMENT. LOW VOLTAGE, PRECORDIAL LEADS. PROBABLE LVH WITH SECONDARY REPOL ABNRM; GR CHEST 2 PROJECTIONS:SUBOPTIMAL INSPIRATION. NO OBVIOUS ACUTE ABNORMALITY.; US ABDOMEN, COMPLETE:UNCOMPLICATED CHOLELITHIASIS. PROBABLE HEPATIC STEATOSIS. OTHERWISE UNREMARKABLE EXAMINATION. SOME TECHNICAL LIMITATION NOTED.; [redacted]20[redacted] (Rx Day 523): ABDOMEN, 2 OR MORE PROECTIONS:PATCHY INTERSTITIAL AND AIRSPACE OPACITIES IN BOTH LUNGS WERE DESCRIBED IN THE PREVIOUS CT SCAN IS MOST LIKELY REPRESENTING ATELECTASIS HOWEVER SUPERIMPOSED INFECTION CANNOT BE EXCLUDED I SUGGEST CLIN; CHEST SUPINE AP:PATCHY INTERSTITIAL AND AIRSPACE OPACITIES IN BOTH LUNGS WERE DESCRIBED IN THE PREVIOUS CT SCAN IS MOST LIKELY REPRESENTING ATELECTASIS HOWEVER SUPERIMPOSED INFECTION CANNOT BE EXCLUDED 1 SUGGEST CLIN; ECG:SINUS RHYTHM. VENTRICULAR PREMATURE COMPLEX. LOW VOLTAGE, PRECORDIAL LEADS. BORDERLINE T ABNORMALITIES, INFERIOR LEADS; [redacted]20[redacted] (Rx Day 526): US ABDOMEN, COMPLETE 2 OR MORE ORGANS:CHOLELITHIASIS AND GALLBLADDER SLUDGE WITH NO FEATURES OF ACUTE CHOLECYSTITIS. LIMITED VISUALIZATION OF TEH CBD WITH NORMAL CALIBER MEASURED AT 3MM. NO INTRAHEPATIC BILIARY DILATATION. MODERATE FATTY

AE Stopped Rx Day	526 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CHEST PAIN AND DIFFICULTY BREATHING RELATED TO PNEUMONIA. NO KNOWN CAUSE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

Event #3: Event of Interest - Hepatic Events

Event Description	FATTY LIVER
Preferred Term	脂肪肝
AE Onset Date / Rx Day	[redacted]20[redacted] / 526 (20 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	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

カナダ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，市中感染性肺炎及び急性腎障害の事象を発現した。

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 15 年間），高血圧，膀胱性尿閉，腎結石及び飲酒者（1 日 2 杯未満）であった。

投与 522 日後，被験者は市中感染性肺炎及び急性腎障害を発現した。投与 526 日後，市中感染性肺炎及び急性腎障害は消失した。

投与 522 日後，被験者は胸痛及び呼吸困難のため，救急治療室を受診した。発熱，筋肉痛及び低酸素症のため，被験者は入院した。COVID-19 の検査は陰性で，COVID-19 のワクチンは接種していなかった。被験者は肺炎と診断され，抗生物質が投与された。臨床検査の結果，軽度の腎不全及び肝酵素の軽度の増加が認められた。投与 526 日後，被験者はすべての症状が完全に消失し，退院した。

治験責任医師によると，肝酵素増加はクレストールの投与に関連するものであった。被験者には，睡眠時無呼吸の既往や検査で確認された肺炎はなかった。

Causality for RISANKIZUMAB (Blinded)

---

1) Community acquired pneumonia (10010120) (Pneumonia (10035664)) [v.23.1] [10010120]

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

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

Dechallenge: Not Applicable

2) Acute kidney injury (10069339) (Acute kidney injury (10069339)) [v.23.1] [10069339]

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 COMMUNITY ACQUIRED PNEUMONIA

- Investigator: Chest pain and difficulty breathing related to pneumonia. No known cause.

- AbbVie: Not applicable

Event of ACUTE KIDNEY INJURY

- Investigator: Likely due to medications given at hospital.

- AbbVie: The event is more likely related to the concurrent pneumonia. Additional risk factors are pre-existing bladder retention and nephrolithiasis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 177 U/L

[redacted] 20[redacted] ALT: 67 U/L

[redacted] 20[redacted] BILIRUBIN: 21 umol/L

[redacted] 20[redacted] BMI: 38.18 kg/m2

[redacted] **20[redacted] CHEST X RAY:** Patchy interstitial and airspace opacities in both lungs were described in the previous CT scan is most likely representing atelectasis, however, superimposed infection cannot be excluded. 1 suggest clinical correlation and radiograph follow-up

[redacted] **20[redacted] COVID-19 TEST:** Nasopharyngeal swab: negative

[redacted] **20[redacted] COVID-19 TEST:** Nasopharyngeal swab: negative

[redacted] 20[redacted] CREATININE: 120 umol/L

[redacted] **20[redacted] CT CHEST:** No evidence of pulmonary embolism. Reduced lung volume with extensive patchy pulmonary opacities favored to be largely related to atelectasis. Superimposed infection or edema is now excluded. Small bilateral pleural effusions.

[redacted] **20[redacted] CXR:** Patchy interstitial airspace disease

[redacted] **20[redacted] ECG:** Sinus Rhythm. Low Voltage, precordial leads. Borderline T abnormalities, inferior leads.

[redacted] **20[redacted] ECG:** Sinus rhythm. Probably left atrial enlargement. Low voltage, precordial leads. Low voltage, precordial leads. Probable LVH with secondary REPOL ABNRM

[redacted] **20[redacted] ECG:** Sinus rhythm. Ventricular premature complex. Probable left ventricular hypertrophy. Borderline T abnormalities, Inferior leads.

[redacted] **20[redacted] ECG:** Sinus rhythm. Ventricular premature complex low voltage, precordial leads. Borderline T abnormalities, inferior leads

[redacted] **20[redacted] GR CHEST 2 PROJECTIONS:** Suboptimal inspiration. No obvious acute abnormality

[redacted] **20[redacted] US ABDOMEN:** Uncomplicated cholelithiasis. Probable hepatic steatosis. Otherwise, unremarkable examination. Some technical limitations noted.

[redacted] **20[redacted] US ABDOMEN:** Cholelithiasis and gallbladder sludge with no features of acute cholecystitis. Limited visualization of the CBD with normal caliber measured at 3mm. No intrahepatic biliary dilation. Moderate fatty infiltration of liver.

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 M16-006 Study Start	Sex	Race
Placebo SC Q8W	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: CHRONIC GASTRODUODENITIS	20[redacted]
ANEMIA: IRON-DEFICIENCY ANEMIA	20
OTHER: POLYOSTEOARTHROSIS	20
CROHN'S DISEASE	20
OTHER: PERIPHERAL ARTHROPATHY	20

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20
SURGERY: ADRECTAL FISTULA	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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /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] / [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] / 246 246	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 303 303	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 359 359	1
PLACEBO	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 414 414	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]
SULFASALAZINE	2 g	QD	Y-M: 20[redacted]
METHOTREXATE	25 mg	OTHER: ONCE A WEEK	Y-M: 20[redacted] / -297

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 Description CROHN'S DISEASE AGGRAVATION

Preferred Term クローン病

AE Onset Date / Rx Day [redacted]20[redacted] / 168

Age at AE Onset 4[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 168): Alanine Aminotransferase: 13 [2 - 55] U/L; Amylase: 41 [25 - 125] U/L; Aspartate Aminotransferase: 15 [5 - 34] U/L; Bilirubin: 5 [3 - 21] UMOL/L; C Reactive Protein: 2.6 [0 - 5] MG/L; Creatinine: 57 [44 - 111] UMOL/L; Glucose: 5.6 [3.5 - 6.1] MMOL/L; Hematocrit: 0.31 [0.36 - 0.48] FRACTION OF 1; Hemoglobin: 108 [120 - 160] G/L; Leukocytes: 6.9 [4 - 9] 10^9/L; Lymphocytes/Leukocytes: 36 [19 - 37] %; Monocytes/Leukocytes: 9 [3 - 11] %; NPTST366-MYELOCYTES: 1 [0 - 0] %; NPTST524-TOTAL PROTEIN: 65 [35 - 50] G/L; Neutrophils/Leukocytes: 54 [48 - 78] %; Platelets: 314 [150 - 400] 10^9/L; Potassium: 3.9 [3.6 - 6.1] MMOL/L; Sodium: 128 [135 - 152] MMOL/L; [redacted]20[redacted] (Rx Day 170): Amylase: 57 [25 - 125] U/L; Erythrocytes: 4.2 [3.9 - 5] 10^12/L; Hematocrit: 0.34 [0.36 - 0.48] FRACTION OF 1; Hemoglobin: 114 [120 - 160] G/L; Leukocytes: 6.7 [4 - 9] 10^9/L; Lymphocytes/Leukocytes: 35 [19 - 37] %; Monocytes/Leukocytes: 9 [3 - 11] %; Neutrophils/Leukocytes: 56 [48 - 78] %; Platelets: 352 [150 - 400] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 168): ABDOMINAL ULTRASOUND:NORMAL; CHEST X-RAY:NORMAL; ECG:NORMAL; GASTRODUODENOSCOPY:NORMAL; X-RAY OF THE ABDOMEN:NORMAL

AE Stopped Rx Day	177
Duration of AE	10 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NA
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 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，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，慢性胃十二指腸炎，肛門直腸瘻，クローン病，非喫煙者及び非飲酒者であった。

投与 168 日後，被験者はクローン病増悪を発現した。投与 177 日後，クローン病増悪は消失した。

投与 168 日後，被験者は，左右腸骨領域で痛みが強い痙攣性腹痛，腹部膨満感，3 日間続く悪心，高体温症（非重篤），浮動性めまい，脱力及び動悸があったため，入院した。診断のため臨床検査及び画像検査が実施された。投与 177 日後，被験者は退院した。

Causality for RISANKIZUMAB (Blinded)

---

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'S DISEASE AGGRAVATION

- Investigator: Not reported.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL ULTRASOUND: NORMAL

[redacted] 20[redacted] ABDOMINAL XRAY: NORMAL

[redacted] **20[redacted] AMYLASE:** 41 U/L (normal 25 to 125)

[redacted] **20[redacted] AMYLASE:** 57 U/L (normal 25 to 125)

[redacted] **20[redacted] BILIRUBIN:** 4.7 MCMOL/L (normal 3.4 to 20.5)

[redacted] 20[redacted] BLOOD PRESSURE: 110/70 mmHg

[redacted] 20[redacted] BODY TEMPERATURE: 36.6 Degrees C

[redacted] 20[redacted] CXR: NORMAL

[redacted] 20[redacted] GASTRODUODENOSCOPY: NORMAL

[redacted] **20[redacted] GLUCOSE:** 5.6 MMOL/L (normal 3.5 to 6.1)

[redacted] **20[redacted] HEMATOCRIT:** 30.7 % (normal 36 to 48)

[redacted] **20[redacted] HEMATOCRIT:** 34.4 % (normal 36 to 48)

[redacted] **20[redacted] HGB:** 108 G/L (normal 120 to 160)

[redacted] **20[redacted] HGB:** 108 G/L (normal 120 to 160)

[redacted] **20[redacted] PLT:** 314 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLT:** 352 X10**9/L (normal 150 to 400)

[redacted] 20[redacted] PULSE: 74 /min

[redacted] 20[redacted] RESPIRATORY RATE: 16 /min

[redacted] **20[redacted] SODIUM:** 127 MMOL/L (normal 135 to 152)

[redacted] 20[redacted] STOOL TEST: Not available

[redacted] **20[redacted] WBC:** 6.93 X10**9/L (normal 6 to 9)

[redacted] **20[redacted] WBC:** 6.74 X10**9/L (normal 6 to 9)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
感染性胸水	X			X
肝膿瘍	X			X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: ARTHRALGIA	20[redacted]
OTHER: ANKYLOSING SPONDYLITIS	20[redacted]
CROHN'S DISEASE	20[redacted]
ANEMIA: ANEMIA	20[redacted]
INFLAMMATORY BOWEL DISEASE: ABDOMINAL MASS RIGHT ILEAC FOSSA RELATED TO IBD ACTIVITY	20[redacted]
OTHER: HEMORRHOID TAGS	20[redacted]
OTHER: VITAMIN D DEFFICIENCY	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	7 CIGARETTE	7	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1

RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 79	[redacted]20[redacted] / 79	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 141	[redacted]20[redacted] / 141	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 194	[redacted]20[redacted] / 194	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 245	[redacted]20[redacted] / 245	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 301	[redacted]20[redacted] / 301	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 357	[redacted]20[redacted] / 357	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 411	[redacted]20[redacted] / 411	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]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 MG. DECREASED PROGRESSIVELY UNTIL 20 MG/DAY IN [redacted]-20[redacted] mg	QD	Y-M: 20[redacted] / -31
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -9

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
POTASSIUM	40 mEq	QD	Y-M: 20[redacted] / 90	Y-M: 20[redacted] / 92
SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 90	Y-M: 20[redacted] / 92
COLECALCIFEROL	0.05 mg	QD	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 107
FUROSEMIDE	40 mg	QD	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 110
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 124
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 124

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

Event Description	HEPATIC ABSCESS, THORACIC EMPIEMA
Preferred Term	感染性胸水
AE Onset Date / Rx Day	[redacted]20[redacted] / 90

Age at AE Onset	3[redacted]
Laboratory Testing	[redacted]20[redacted] (Rx Day 90): Activated Partial Thromboplastin Time: 29 [0 - 29] SEC; Alanine Aminotransferase: 10 [10 - 33] U/L; Albumin: 24 [35 - 52] G/L; Alkaline Phosphatase: 157 [35 - 105] U/L; Aspartate Aminotransferase: 10 [0 - 32] U/L; Bilirubin: 4 [0 - 21] UMOL/L; C Reactive Protein: 2380 [0 - 5] MG/L; Creatinine: 57 [44 - 80] UMOL/L; Eosinophils: 0.02 [0 - 0.5] 10^9/L; Hemoglobin: 8 [12 - 15] G/L; Leukocytes: 15 [4 - 11] 10^9/L; Neutrophils: 12.6 [1.9 - 7.5] 10^9/L; Platelets: 899 [150 - 450] 10^9/L; Prothrombin Time: 18 [0 - 12] SEC; [redacted]20[redacted] (Rx Day 92): C Reactive Protein: 230 [5 - NOT REPORTED] mg/L; Hemoglobin: 9 [12 - 15] G/L; Leukocytes: 16.6 [4 - 11] 10^9/L; Neutrophils: 14.79 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 96): C Reactive Protein: 166 [5 - NOT REPORTED] mg/L; Hemoglobin: 83 [120 - 153] G/L; Leukocytes: 12.4 [4 - 11] 10^9/L; Neutrophils: 11.1 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 99): C Reactive Protein: 104 [5 - NOT REPORTED] mg/L; Hemoglobin: 85 [120 - 153] G/L; Leukocytes: 13.4 [4 - 11] 10^9/L; Neutrophils: 10.92 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 103): C Reactive Protein: 101 [5 - NOT REPORTED] mg/L; Hemoglobin: 74 [120 - 153] G/L; Leukocytes: 12.1 [4 - 11] 10^9/L; Neutrophils: 11.07 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 107): C Reactive Protein: 156 [5 - NOT REPORTED] mg/L; Hemoglobin: 75 [120 - 153] G/L; Leukocytes: 8.7 [4 - 11] 10^9/L; Neutrophils: 6.28 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 110): C Reactive Protein: 84 [5 - NOT REPORTED] mg/L; Hemoglobin: 91 [120 - 153] G/L; Leukocytes: 9.4 [4 - 11] 10^9/L; Neutrophils: 6.95 [1.9 - 7.5] 10^9/L
Microbiology	[redacted]20[redacted] (Rx Day 90): URINE CULTURE URINE: Negative; BLOOD CULTURE, AEROBIC AND ANAEROBIC: Negative; [redacted]20[redacted] (Rx Day 91): OTHER HEPATIC ABSCESS CULTURE: Positive-PROTEUS MIRABILIS,STREPTOCOCCUS ANGINOSUS, BACTEROIDES FRAGILIS; OTHER PLEURAL EFFUSION, CULTURE PLEURAL EFFUSION, CULTURE: Negative; [redacted]20[redacted] (Rx Day 95): BLOOD CULTURE: Negative; [redacted]20[redacted] (Rx Day 96): OTHER PLEURAL EFFUSION, CULTURE PLEURAL EFFUSION, CULTURE: Negative; [redacted]20[redacted] (Rx Day 100): OTHER HEPATIC ABSCESS PUS: Positive-E.COLI, PROTEUS MIRABILIS, BACTEROIDES FRAGILIS; [redacted]20[redacted] (Rx Day 103): OTHER PUS, HEPATIC ABSCESS CULTURE: Positive-BACTEROIDES FRAGILIS; BLOOD CULTURE BLOOD: Negative; [redacted]20[redacted] (Rx Day 106): OTHER HEPATIC ABCESS CULTURE: Negative; [redacted]20[redacted] (Rx Day 108): BLOOD CULTURE: Negative; [redacted]20[redacted] (Rx Day 113): OTHER DRAINAGE OF HEPATIC ABSCESS CULTURE OF PUS: Negative
SAE Supplemental Procedure	[redacted]20[redacted] (Rx Day 90): CT SCAN:MULTIPLE HEPATIC ABCESSES; PLEURAL EFFUSION; [redacted]20[redacted] (Rx Day 91): [redacted]-[redacted]-20[redacted]. PERCUTANEOUS DRAINAGE OF HEPATIC ABSCESS:PERCUTANEOUS DRAINAGE OF HEPATIC ABSCESS; THORACOCENTESIS [redacted]-[redacted]-20[redacted]:THORACOCENTESIS [redacted]-[redacted]-20[redacted]; [redacted]20[redacted] (Rx Day 96): THORACOCENTESIS [redacted]-[redacted]-20[redacted]:THORACOCENTESIS [redacted]-[redacted]-20[redacted]; [redacted]20[redacted] (Rx Day 100): DRAINAGE OF HEPATIC ABSECC 8-[redacted]-20[redacted]:DRAINAGE OF HEPATIC ABSECC [redacted]-[redacted]-20[redacted]; [redacted]20[redacted] (Rx Day 103): [redacted]-[redacted]-20[redacted] DRAINAGE OF HEPATIC ABSCESS:[redacted]-[redacted]-20[redacted] DRAINAGE OF HEPATIC ABSCESS; [redacted]20[redacted] (Rx Day 113): [redacted]-[redacted]-20[redacted] DRAINAGE OF HEPATIC ABSCESS:[redacted]-[redacted]-20[redacted] DRAINAGE OF HEPATIC ABSCESS; [redacted]-[redacted]-20[redacted] THORACOCENTESIS:[redacted]-[redacted]-20[redacted] THORACOCENTESIS
AE Stopped Rx Day	124
Duration of AE	35 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOTE THAT ANY OF THE DRUGS (PREDNISOLONE, AZATHIOPRINE, STUDY DRUG) CAN INCREASE THE RISK OF INFECTIONS
Discontinued Study Drug Due to the Event	NO

SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

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

Event Description	HEPATIC ABSCESS, THORACIC EMPIEMA
Preferred Term	肝膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 90
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 90): Activated Partial Thromboplastin Time: 29 [0 - 29] SEC; Alanine Aminotransferase: 10 [10 - 33] U/L; Albumin: 24 [35 - 52] G/L; Alkaline Phosphatase: 157 [35 - 105] U/L; Aspartate Aminotransferase: 10 [0 - 32] U/L; Bilirubin: 4 [0 - 21] UMOL/L; C Reactive Protein: 2380 [0 - 5] MG/L; Creatinine: 57 [44 - 80] UMOL/L; Eosinophils: 0.02 [0 - 0.5] 10^9/L; Hemoglobin: 8 [12 - 15] G/L; Leukocytes: 15 [4 - 11] 10^9/L; Neutrophils: 12.6 [1.9 - 7.5] 10^9/L; Platelets: 899 [150 - 450] 10^9/L; Prothrombin Time: 18 [0 - 12] SEC; [redacted]20[redacted] (Rx Day 92): C Reactive Protein: 230 [5 - NOT REPORTED] mg/L; Hemoglobin: 9 [12 - 15] G/L; Leukocytes: 16.6 [4 - 11] 10^9/L; Neutrophils: 14.79 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 96): C Reactive Protein: 166 [5 - NOT REPORTED] mg/L; Hemoglobin: 83 [120 - 153] G/L; Leukocytes: 12.4 [4 - 11] 10^9/L; Neutrophils: 11.1 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 99): C Reactive Protein: 104 [5 - NOT REPORTED] mg/L; Hemoglobin: 85 [120 - 153] G/L; Leukocytes: 13.4 [4 - 11] 10^9/L; Neutrophils: 10.92 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 103): C Reactive Protein: 101 [5 - NOT REPORTED] mg/L; Hemoglobin: 74 [120 - 153] G/L; Leukocytes: 12.1 [4 - 11] 10^9/L; Neutrophils: 11.07 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 107): C Reactive Protein: 156 [5 - NOT REPORTED] mg/L; Hemoglobin: 75 [120 - 153] G/L; Leukocytes: 8.7 [4 - 11] 10^9/L; Neutrophils: 6.28 [1.9 - 7.5] 10^9/L; [redacted]20[redacted] (Rx Day 110): C Reactive Protein: 84 [5 - NOT REPORTED] mg/L; Hemoglobin: 91 [120 - 153] G/L; Leukocytes: 9.4 [4 - 11] 10^9/L; Neutrophils: 6.95 [1.9 - 7.5] 10^9/L

Microbiology

[redacted]20[redacted] (Rx Day 90): URINE CULTURE URINE: Negative; BLOOD CULTURE, AEROBIC AND ANAEROBIC: Negative; [redacted]20[redacted] (Rx Day 91): OTHER HEPATIC ABSCESS CULTURE: Positive-PROTEUS MIRABILIS,STREPTOCOCCUS ANGINOSUS, BACTEROIDES FRAGILIS; OTHER PLEURAL EFFUSION, CULTURE PLEURAL EFFUSION, CULTURE: Negative; [redacted]20[redacted] (Rx Day 95): BLOOD CULTURE: Negative; [redacted]20[redacted] (Rx Day 96): OTHER PLEURAL EFFUSION, CULTURE PLEURAL EFFUSION, CULTURE: Negative; [redacted]20[redacted] (Rx Day 100): OTHER HEPATIC ABSCESS PUS: Positive-E.COLI, PROTEUS MIRABILIS, BACTEROIDES FRAGILIS; [redacted]20[redacted] (Rx Day 103): OTHER PUS, HEPATIC ABSCESS CULTURE: Positive-BACTEROIDES FRAGILIS; BLOOD CULTURE BLOOD: Negative; [redacted]20[redacted] (Rx Day 106): OTHER HEPATIC ABCESS CULTURE: Negative; [redacted]20[redacted] (Rx Day 108): BLOOD CULTURE: Negative; [redacted]20[redacted] (Rx Day 113): OTHER DRAINAGE OF HEPATIC ABSCESS CULTURE OF PUS: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 90): CT SCAN:MULTIPLE HEPATIC ABCESSES; PLEURAL EFFUSION; [redacted]20[redacted] (Rx Day 91): [redacted]-20[redacted]. PERCUTANEOUS DRAINAGE OF HEPATIC ABSCESS:PERCUTANEOUS DRAINAGE OF HEPATIC ABSCESS; THORACOCENTESIS [redacted]-20[redacted]:THORACOCENTESIS [redacted]-20[redacted]; [redacted]20[redacted] (Rx Day 96): THORACOCENTESIS [redacted]-20[redacted]:THORACOCENTESIS [redacted]-20[redacted]; [redacted]20[redacted] (Rx Day 100): DRAINAGE OF HEPATIC ABSECC [redacted]-20[redacted]:DRAINAGE OF HEPATIC ABSECC [redacted]-20[redacted]; [redacted]20[redacted] (Rx Day 103): [redacted]-20[redacted] DRAINAGE OF HEPATIC ABSCESS:[redacted]-20[redacted] DRAINAGE OF HEPATIC ABSCESS; [redacted]20[redacted] (Rx Day 113): [redacted]-20[redacted] DRAINAGE OF HEPATIC ABSCESS:[redacted]20[redacted] DRAINAGE OF HEPATIC ABSCESS; [redacted]-20[redacted] THORACOCENTESIS:[redacted]-20[redacted] THORACOCENTESIS

AE Stopped Rx Day	124
Duration of AE	35 DAYS
Severity	SEVERE

Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOTE THAT ANY OF THE DRUGS (PREDNISOLONE, AZATHIOPRINE, STUDY DRUG) CAN INCREASE THE RISK OF INFECTIONS
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

ポルトガル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，肝膿瘍及び膿胸の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，クローン病，貧血，炎症性腸疾患活動に関連する右回腸窩腹部腫瘤，喫煙者（1 日 7 本を 7 年間）及び非飲酒者であった。

投与 90 日後，被験者は肝膿瘍及び膿胸を発現した。投与 124 日後，肝膿瘍及び膿胸は消失した。

投与 90 日後，被験者は右下胸郭の肺音がなく，腹部の膨満及び圧痛，両下肢浮腫及び発熱があり，来院した。被験者は肝膿瘍及び膿胸と診断された。入院中，肝膿瘍の経皮的ドレナージが数回，胸腔穿刺が 2 回行われた。投与 124 日後，被験者は退院した。

治験責任医師によると，被験者には低体重のリスク因子があった。

肝膿瘍及び膿胸は，被験者が M16-000 試験を開始した後に発現したことが治験責任医師によって確認された（M16-006 試験下で情報を入手済であった）。本症例において，[redacted] の情報がすべて入手された。

投与された薬剤は，セフトリアキソン，メトロニダゾール，アモキシシリン・クラブラン酸合剤及びピペラシリン・タゾバクタム合剤であった。

The patient's past medications include:

HUMIRA for CROHN'S DISEASE ([redacted])

INFLECTRA for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Pulmonary empyema (10037381) (Infectious pleural effusion (10071699)) [v.23.1] [10037381]

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

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

Dechallenge: Not Applicable

2) Liver abscess (10024652) (Liver abscess (10024652)) [v.23.1] [10024652]

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 HEPATIC ABSCESS, THORACIC EMPYEMA

- Investigator: Note that any of the drugs (Prednisolone, Azathioprine, study drug) can increase the risk of infections.

- AbbVie: Event of hepatic abscess is more likely a complication of Crohn's disease and event of empyema is more likely related to concurrent hepatic abscess, additional risk factor includes current smoking status.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL ULTRASOUND:** Catheter is adequately positioned; abscess is 14X5.2cm

[redacted] 20[redacted] ABSCESS MICROBIOLOGY: Negative

[redacted] 20[redacted] ACTIVATED PARTIAL THROMBOPLASTIN TIME: 29.3 SEC (normal 0 to 29)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 10 U/L (normal 10 to 53)

[redacted] **20[redacted] ALBUMIN:** 2.4 G/DL (normal 3.5 to 5.2)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 10 U/L (normal 0 to 32)

[redacted] **20[redacted] BILIRUBIN:** 0.23 mg/dL (normal 0 to 1.2)

[redacted] **20[redacted] BLOOD CULTURE:** Aerobe, Anaerobe- Negative

[redacted] 20[redacted] BLOOD CULTURE: Negative

[redacted] 20[redacted] BLOOD CULTURE: Negative

[redacted] 20[redacted] BLOOD CULTURE: Negative

[redacted] 20[redacted] BODY TEMPERATURE: 39.5 Degrees C

[redacted] **20[redacted] COMPUTED TOMOGRAPHY:**Multiple hepatic abscesses, pleural effusion

[redacted] **20[redacted] CREATININE:** 0.64 mg/dL (normal 0.5 to 0.9)

[redacted] **20[redacted] CULTURE:** Hepatic abscess: positive- Proteus Mirabilis, Streptococcus Anginosus, Bacteroides Fragilis

[redacted] **20[redacted] CULTURE:** Pleural effusion: Negative

[redacted] **20[redacted] CULTURE:** Pleural effusion: Negative

[redacted] **20[redacted] CULTURE:** Pus hepatic abscess: Positive- E. Coli, Proteus Mirabilis, Bacteroides Fragilis.

[redacted] **20[redacted] CULTURE:** Hepatic abscess: Negative

[redacted] **20[redacted] EOSINOPHILS ABS:** 0.02 X10**9/L (normal 0 to 0.45)

[redacted] **20[redacted] HEMOGLOBIN:** 7.7 G/DL (normal 12 to 15.3)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 238 MG/L (normal 0 to 5)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 157 U/L (normal 35 to 105)

[redacted] **20[redacted] NEUTROPHILS ABS:** 12.650 X10**9/L (normal 1.9 to 9.5)

[redacted] **20[redacted] PLATELET COUNT:** 899 X10**9/L (normal 150 to 450)

[redacted] **20[redacted] PROTHROMBIN TIME:** 18.2 SEC (normal 0 to 11.6)

[redacted] 20[redacted] THORACENTESIS MICROBIOLOG: Negative

[redacted] 20[redacted] URINE CULTURE: Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 15 X10**9/L (normal 4 to 11)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
クローン病	X			
下痢	X			
坐骨神経痛	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: ANEMIA IN CHRONIC DIESASE	NOT REPORTED
CHOLELITHIASIS: STATUS POST CHOLECYSTECTOMIAM	NOT REPORTED
EYE DISEASE/DISORDER: CATARACT	NOT REPORTED
LIVER DISEASE (EXCLUDING HEPATITIS): STEATOSIS HEPATIS (NAFLD)	NOT REPORTED
ANGINA	19[redacted]
HYPERTENSION	19[redacted]
HYPERTHYROIDISM	19[redacted]
DEPRESSION: ANXIETY	19[redacted]
OTHER: POST MENOPAUSAL STATUS	20[redacted]
DEPRESSION: F32.2	20[redacted]
CROHN'S DISEASE	20[redacted]
DIABETES MELLITUS	20[redacted]
INFLAMMATORY BOWEL DISEASE: ENTEROCOLITIS PER CLOSTRIDIUM DIFFICILE	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CHOLECYSTECTOMY	19[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
SURGERY: OPERATIO: O DEX PHACO	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 36	[redacted]20[redacted] / 36	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 36	[redacted]20[redacted] / 36	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 153	[redacted]20[redacted] / 153	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 153	[redacted]20[redacted] / 153	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 215	[redacted]20[redacted] / 215	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 215	[redacted]20[redacted] / 215	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 224	[redacted]20[redacted] / 224	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 272	[redacted]20[redacted] / 272	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] / 369	[redacted]20[redacted] / 369	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 432	[redacted]20[redacted] / 432	1
INTERRUPTION			Every 8 Weeks	[redacted]20[redacted] / 595	[redacted]20[redacted] / 624	30

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
MESALAZINE	1 g	OTHER: 4 TIMES PER DAY	Y-M: 20[redacted]
BISOPROLOL	5 mg	QD	Y-M: 20[redacted]
THIAMAZOLE	5 mg	QD	Y-M: 20[redacted]

GLIMEPIRIDE	1 mg	QD	Y-M: 20[redacted]
FOSINOPRIL	20 mg	QD	Y-M: 20[redacted] / -192
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted] / -147
COSOPT	2 OTHER: DROPS	BID	Y-M: 20[redacted] / -37
ACETAZOLAMIDE	125 mg	BID	Y-M: 20[redacted] / 67
ASCORBIC ACID	500 mg	BID	Y-M: 20[redacted] / 67
MAGNESIUM	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / 67
POTASSIUM	1 OTHER: SATCHEL	TID	Y-M: 20[redacted] / 67

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
ACETAZOLAMIDE	125 mg	BID	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 117
ASCORBIC ACID	500 mg	BID	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 117
MAGNESIUM	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 117
POTASSIUM	1 OTHER: SATCHEL	TID	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 117
BROMAZEPAM	1.5 mg	BID	Y-M: 20[redacted] / 117	NOT REPORTED
FOLIC ACID	5 mg	BID	Y-M: 20[redacted] / 117	NOT REPORTED
IRON	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / 117	NOT REPORTED
METFORMIN	1000 mg	BID	Y-M: 20[redacted] / 117	NOT REPORTED
MYDOCALM	150 mg	BID	Y-M: 20[redacted] / 117	NOT REPORTED
PREGABALIN	75 mg	QD	Y-M: 20[redacted] / 117	NOT REPORTED
RAMIPRIL	5 mg	BID	Y-M: 20[redacted] / 117	NOT REPORTED
PARACETAMOL	1000 mg	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 122
RINGER AGUETTANT	500 mg	QD	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 127
METAMIZOLE	1000 mg	QD	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 127
LERCANIDIPINE	10 mg	QD	Y-M: 20[redacted] / 148	NOT REPORTED
FENTANYL	1 mg	QD	Y-M: 20[redacted] / 461	Y-M: 20[redacted] / 461
MIDAZOLAM	1.5 mg	QD	Y-M: 20[redacted] / 461	Y-M: 20[redacted] / 461

PROPOFOL	150 mg	QD	Y-M: 20[redacted]- / 461	Y-M: 20[redacted]- / 461

Event #1: Serious Adverse Event

Event Description	LUMBOISHIALGIA LAT SIN.
Preferred Term	坐骨神経痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 92
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 117): Alkaline Phosphatase: 134 [30 - 120] U/L; C Reactive Protein: 12.3 [0 - 5] MG/L; Cholesterol: 7.3 [3.6 - 5.2] MMOL/L; Glucose: 8 [4.1 - 5.9] MMOL/L; NPTST236-GAMA GLUTAMIL TRANSFERAZA: 80 [0 - 38] U/L; NPTST264-HBA1C (%): 6.3 [4 - 6] %; NPTST265-HBA1C (MMOL/MOL): 46 [20 - 42] MMOL/MOL; NPTST483-SEDIMENTATION: 85 [5 - 28] MM/H; Triglycerides: 2.6 [0.4 - 1.7] MMOL/L

Microbiology

[redacted]20[redacted] (Rx Day 117): STOOL STOOL SAMPLE TAKEN FOR SALMONEL: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 118): ABDOMINAL ULTRASOUND:STEATOSIS HEPATIS; [redacted]20[redacted] (Rx Day 123): CT OF LS SPINE:L4-L5 DECREASED LEVEL OF IV SPACE WITH BALGING OF DISCUSE, L5-S1 DECREASED LEVEL OF IV SPACE WITH DORSAL PROTRUSION OF DISCUS WITH COMPRESION TOWARDS DURAL SACCULUS WITHOUT COMPRESSION OF NEURAL RADIC

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DORSAL PROTRUSION OF VERTEBAL DISCUS L5-S1
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	DIARRHEA
Preferred Term	下痢
AE Onset Date / Rx Day	[redacted]20[redacted] / 107
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 117): Alkaline Phosphatase: 134 [30 - 120] U/L; C Reactive Protein: 12.3 [0 - 5] MG/L; Cholesterol: 7.3 [3.6 - 5.2] MMOL/L; Glucose: 8 [4.1 - 5.9] MMOL/L; NPTST236-GAMA GLUTAMIL TRANSFERAZA: 80 [0 - 38] U/L; NPTST264-HBA1C (%): 6.3 [4 - 6] %; NPTST265-HBA1C (MMOL/MOL): 46 [20 - 42] MMOL/MOL; NPTST483-SEDIMENTATION: 85 [5 - 28] MM/H; Triglycerides: 2.6 [0.4 - 1.7] MMOL/L

Microbiology

[redacted]20[redacted] (Rx Day 117): STOOL STOOL SAMPLE TAKEN FOR SALMONEL: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 118): ABDOMINAL ULTRASOUND:STEATOSIS HEPATIS; [redacted]20[redacted] (Rx Day 123): CT OF LS SPINE:L4-L5 DECREASED LEVEL OF IV SPACE WITH BALGING OF DISCUSE, L5-S1

DECREASED LEVEL OF IV SPACE WITH DORSAL PROTRUSION OF DISCUS WITH COMPRESION TOWARDS DURAL SACCULUS WITHOUT COMPRESSION OF NEURAL RADIC

AE Stopped Rx Day	127
Duration of AE	21 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	USE OF ANELGETICS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	EXARBATION OF CD
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 134
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 136): C Reactive Protein: 15.8 [0 - 5] MG/L; NPTST312-KALIUM: 5.4 [3.5 - 5] MMOL/L; NPTST371-NATRIUM: 149.1 [135 - 145] MMOL/L; [redacted]20[redacted] (Rx Day 137): Glucose: 8.7 [4.1 - 5.9] MMOL/L; Hemoglobin: 118 [119 - 157] G/L; NPTST220-FE: 10.1 [10.7 - 32.2] UMOL/L; NPTST236-GAMA GLUTAMIL TRANSFERAZA: 239 [0 - 38] U/L; NPTST358-MPV: 10.6 [6.8 - 10.4] FL; [redacted]20[redacted] (Rx Day 145): C Reactive Protein: 19.6 [0 - 5] MG/L; NPTST231-FT4: 20.67 [11.5 - 22.7] PMOL/L; NPTST264-HBA1C (%): 6.7 [4 - 6] %; NPTST483-SEDIMENTATION: 95 [5 - 28] MM/H; Thyrotropin: 0.23 [0.4 - 4] MIU/L

Microbiology

[redacted]20[redacted] (Rx Day 137): STOOL STOOL MICROBIOLOGY TEST: Negative-C.DIFFICILE

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	148
Duration of AE	15 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	EXARBATION OF CD DUE TO POSSIBALY OF INEFFECTIVE DRUG
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

セルビア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，坐骨神経痛及び下痢の事象を発現した。

Event 1及び2の臨床経過：

関連する病歴は，甲状腺機能亢進症，クローン病，クロストリジウム・ディフィシレによる腸炎，慢性疾患の貧血，非喫煙者及び非飲酒者であった。

投与92日後，被験者は坐骨神経痛を発現した。投与107日後，被験者は下痢を発現した。投与127日後，下痢は消失した。

投与117日後，被験者は頻回の液状便（24時間に7～8回），疲労及び左股関節部の重度の疼痛のため入院した。下痢に対して対症療法が施された。投与123日後，被験者は，左股関節部に変形性股関節症（非重篤）を発現した。左股関節部の疼痛に対して鎮痛薬が投与された。入院中，排便の回数は減少し，血液の混じらない半液状便が3～4回であった。左鼡径部の疼痛も軽減した。神経科医による診察が行われ，腰仙椎部のCT検査が指示された。投与123日後，CT検査が実施された。投与127日後，被験者は退院した。

投与された薬剤は，Analgin，Midocalm，Pregabalin Mylan及びparacetamolであった。

The patient's past medications include:

PARACETAMOL for PAIN IN THE LEFT HIP ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Lumboischialgia (10049756) (Sciatica (10039674)) [v.22.1] [10049756]

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

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

Dechallenge: Not Applicable

2) Diarrhea (10012727) (Diarrhoea (10012735)) [v.22.1] [10012727]

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 LUMBOISHIALGIA LAT SIN

- Investigator: DORSAL PROTRUSION OF VERTEBAL DISCUS L5-S1

- AbbVie: Event more likely related to spine pathology noted on CT, risk factors include subject's age, obesity and pre-existing crohn's disease. Additionally, extra-intestinal manifestations of inflammatory bowel disease are seen in 25 to 40% of these patients. Inflammatory manifestations of joints, skin, eyes and liver are considered primary extra-intestinal manifestations.

Event of DIARRHEA

- Investigator: USE OF ANELGETICS.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL ULTRASOUND: steatosis hepatis

[redacted] **20[redacted] ALK PHOS:** 134 U/L (normal 30 to 120)

[redacted] **20[redacted] CHOLESTEROL:** 7.3 MMOL/L (normal 3.6 to 5.2)

[redacted] **20[redacted] CT OF LS SPINE:** L4-L5 DECREASED LEVEL F IV SPACE WITH ALGING OF DISCUSE, 5-S1 DECREASED LEVEL F IV SPACE WITH dosal with compresson towards dural sacculus without compression of neural radics

[redacted] **20[redacted] GGT:** 80 U/L (normal 0 to 38)

[redacted] **20[redacted] GLUCOSE:** 8 MMOL/L (normal 4.1 to 5.9)

[redacted] **20[redacted] HBA1C:** 6.3 mol/mol (normal 4 to 6)

[redacted] 20[redacted] HIGH SENSITIVITY CRP: 12.3 MG/L (normal 0 to 5)

[redacted] **20[redacted] SEDIMENTATION RATE:** 85 mm/3.6KS (normal 5 to 28)

[redacted] **20[redacted] STOOL CULTURE:** stool sample taken for salmonelle i shigelle and campylobacter clostridium difficile- negative

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

セルビア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，クローン病増悪の事象を発現した。

Event 3 の臨床経過：

関連する病歴は，クローン病，貧血，非喫煙者及び非飲酒者であった。

投与 134 日後，被験者はクローン病増悪を発現した。投与 148 日後，クローン病増悪は消失した。

本事象発現前，被験者は投与 92 日後に坐骨神経痛（関節痛）を発現し，投与 107 日後に下痢を発現した（AER [redacted]）。

投与 136 日後，被験者は下痢の悪化，腹痛及び貧血の悪化があったため，入院した。被験者は液状便が頻回にあり，極度に消耗していた。入院中，液状便の回数及び疼痛の発現回数は減少した。治験モニターとの協議の結果，ブデソニド 9 mg の投与が開始された。投与 148 日後，被験者は退院した。

本事象に関連するリスク因子は，クローン病であった。

投与された薬剤は，ブデゾニドであった。

The patient's past medications include:

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

HUMA ZOLAMIDE for CATARACT ([redacted] 20[redacted] - [redacted] 20[redacted])

OPTINERVE for PROPHYLAXIS OPTICAL NERVE DAMAGE ([redacted] 20[redacted] - [redacted] 20[redacted])

POTASSIUM for CORRECTION OF HYPOKALEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

VITAMIN C for PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PARACETAMOL for PAIN IN THE LEFT HIP ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

RINGER SOL for DIARRHEA ([redacted] 20[redacted] - [redacted] 20[redacted])

ANALGIN for PAIN IN THE LEFT HIP ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Crohn's aggravated (10011399) (Crohn's disease (10011401)) [v.22.1] [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 EXACERBATION OF CD

- Investigator: Exacerbation due to possibility of ineffective drug.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL ULTRASOUND: Steatosis hepatis.

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 134 U/L (normal 30 to 120)

[redacted] **20[redacted] CHOLESTEROL:** 7.3 MMOL/L (normal 3.6 to 5.2)

[redacted] **20[redacted] CT OF LS SPINE:** L4-L5 decreased level of IV space with bulging of discs, L5-S1 decreased level of IV space with dorsal protrusion of discus with compression towards dural sacculus without compression of neural radics.

[redacted] **20[redacted] FT4:** 20.67 PMOL/L (normal 11.5 to 22.7)

[redacted] 20[redacted] GAMA GLUTAMIL TRANSFERAZA: 239 U/L (normal 0 to 38)

[redacted] **20[redacted] GLUCOSE:** 8.0 MMOL/L (normal 4.1 to 5.9)

[redacted] **20[redacted] GLUCOSE:** 8.7 MMOL/L (normal 4.1 to 5.9)

[redacted] **20[redacted] HBA1:** 6.7 % (normal 4 to 6)

[redacted] **20[redacted] HBA1C:** 6.3 % (normal 4 to 6)

[redacted] **20[redacted] HBA1C:** 46 MMOL/MOL (normal 20 to 42)

[redacted] **20[redacted] HEMOGLOBIN:** 118 G/L (normal 119 to 157)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 15.8 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 19.6 MG/L (normal 0 to 5)

[redacted] **20[redacted] IRON:** 10.1 umol/L (normal 10.7 to 32.2)

[redacted] **20[redacted] KALIUM:** 5.4 MMOL/L (normal 3.5 to 5)

[redacted] **20[redacted] MPV:** 10.6 FL (normal 6.8 to 10.4)

[redacted] **20[redacted] NATRIUM:** 149.1 MMOL/L (normal 135 to 145)

[redacted] **20[redacted] SEDIMENTATION:** 95 mm/h (normal 5 to 28)

[redacted] 20[redacted] STOOL SAMPLE TAKEN FOR CLOSTRIDIUM DIFFICILE: Negative.

[redacted] 20[redacted] THYROID STIMULATING HORMONE: 0.234 mIU/L (normal 0.4 to 4)

[redacted] **20[redacted] TRIGLYCERIDES:** 2.6 MMOL/L (normal 0.4 to 1.7)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at M16-006 Study Start	Sex	Race
Placebo SC Q8W	2[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
LATENT TUBERCULOSIS	NOT REPORTED
OBESITY	20[redacted]
CLOTTING/BLEEDING PROBLEMS: PORTAL VEIN THROMBOSIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: CROHN'S ILEITIS	20[redacted]
OTHER: ORAL ULCERS	20[redacted]
CROHN'S DISEASE	20[redacted]
TUBERCULOSIS: LATENT TB	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	1 CIGARETTE	8	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1

M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 57 57	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 57 57	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

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]
WARFARIN	10 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
CALCIUM	500 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	500 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	50000 ug	QD	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted]
PREDNISONE	60 mg	QD	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -70
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -6
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -2

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
WARFARIN	10 mg	QD	Y-M: 20[redacted]	ONGOING
CALCIUM	500 mg	QD	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	500 mg	QD	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	50000 ug	QD	Y-M: 20[redacted]	ONGOING
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -70	ONGOING
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -2	ONGOING

Event #1: Serious Adverse Event

Event Description	TERMINATION OF PREGNANCY
Preferred Term	人工流産
AE Onset Date / Rx Day	[redacted]20[redacted] / 213 (72 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 213): TERMINATION OF PREGNANCY:PREGNANCY TERMINATED

AE Stopped Rx Day	213 (72 DAYS AFTER LAST TREATMENT)
Duration of AE	1 DAY
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ELECTIVE TERMINATION OF PREGNANCY
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

南アフリカ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，妊娠中絶及び妊娠時の母体の曝露（非重篤）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，肥満，クローン回腸炎，クローン病，潜伏結核，喫煙者（1 日 1 本を 8 年間）及び飲酒者（1 日 2 杯未満）であった。

妊娠時の母体の曝露が発現した（日付不明）。投与 213 日後，被験者は妊娠中絶を発現した。投与 213 日後，妊娠中絶は消失した。

被験者は計画外妊娠をした（日付不明）。報告時の胎児の推定在胎週数（EGA）は不明であった。分娩予定日（EDD）は投与から約 15 ヵ月後であった。胎児は，妊娠前及び妊娠初期にリサンキズマブの母体使用に曝露（子宮内）された。被験者は避妊法を使用しておらず，禁欲法を使用していた。胎児に障害はなかったか，不明であった。投与 213 日後，被験者は選択的中絶を受けた。被験者は母親に知られたくなかったため，治験実施医療機関への妊娠の報告を躊躇していた。治験責任医師に妊娠が報告され，リサンキズマブの投与は一時中止された。

The patient's past medications include:

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

Causality for RISANKIZUMAB (Blinded)

---

1) Termination of pregnancy (10043281) (Abortion induced (10000220)) [v.23.1] [10043281]

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) Maternal exposure during pregnancy (10071408) (Maternal exposure during pregnancy (10071408)) [v.23.1] [10071408]

Causality as per reporter (Drug/Vaccine): Not Reported

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

Dechallenge: No

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of TERMINATION OF PREGNANCY

- Investigator: Elective termination of pregnancy

- AbbVie: Event is more likely related to the subject's choice to terminate the pregnancy.

Event of MATERNAL EXPOSURE DURING PREGNANCY

- Investigator:

- AbbVie: Special situation of maternal use of active pharmaceutical ingredient.

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 M16-006 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	2[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
LATENT TUBERCULOSIS	NOT REPORTED
ASTHMA	19[redacted]
OTHER: LOWER BACK PAIN	20[redacted]
OSTEOARTHRITIS: HANDS & FEET JOINTS	20[redacted]
OTHER: BELOW ANKLE OEDEMA	20[redacted]
OTHER: IRRITABLE BOWEL SYNDROME	20[redacted]
OTHER: INTERMITTENT FACIAL RASH	20[redacted]
OTHER: RECURRENT URINARY TRACT INFECTION	20[redacted]
CROHN'S DISEASE	20[redacted]
EYE DISEASE/DISORDER: INTERMITTED BLURRY VISIT	20[redacted]
OTHER: INTERMITTENT HEADACHES	20[redacted]
ANEMIA: RECURRENT	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: GALLSTONES	20[redacted]
OTHER: RECURRING CYSTS ON LEFT OVARY	20[redacted]
OTHER: MIGRAINE	20[redacted]

Prior Procedures	Procedure Year
SURGERY: DRAINAGE OF FLUID BOTH KNEES	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]
SURGERY: DRAINAGE OVARIAN CYST	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
SURGERY: LEFT OVARIECTOMY	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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 25	[redacted] / 25	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 25	[redacted] / 25	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 53	[redacted] / 53	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 53	[redacted] / 53	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 81	[redacted] / 81	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 137	[redacted] / 137	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 193	[redacted] / 193	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted] / 221	[redacted] / 221	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 242	[redacted] / 242	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 305	[redacted] / 305	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 361	[redacted] / 361	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 417	[redacted] / 417	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]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]

DIENOGEST	2 mg	QD	Y-M: 20[redacted] / -352
INTRAVAGINAL CONTRACEPTIVES	1 OTHER: 1	PRN	Y-M: 20[redacted] / -352

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
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / 149	NOT REPORTED
BLOOD AND RELATED PRODUCTS	2 OTHER: UNITS	OTHER: STAT	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 165
FUROSEMIDE	20 mg	PRN	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 165
ONDANSETRON	4 mg	TID	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 165
TRAMADOL	100 mg	TID	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 165
BALSOLENE	1000 mL	PRN	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 166
IRON	1200 mg	OTHER: STAT	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 165
PANTOPRAZOLE	80 mg	OTHER: STAT	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 165
PETHIDINE	50 mg	OTHER: STAT	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 165
MERSYNDOL	2 OTHER: TABLETS	QD	Y-M: 20[redacted] / 189	NOT REPORTED

Event #1: Serious Adverse Event

Event Description	ANAEMIA
Preferred Term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 151
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 164): Ery. Mean Corpuscular Hemoglobin: 21.2 [27 - 32] PG; Hematocrit: 0.33 [0.37 - 0.49] FRACTION OF 1; Hemoglobin: 98 [121 - 163] G/L; NPTST001-% SATURATION: 5 [15 - 50] %; NPTST224-FERRITIN: 4 [13 - 150] NG/ML; NPTST310-IRON: 4 [9 - 30.4] UMOL/L; NPTST334-MCHC: 29.9 [31 - 37] G/DL; Platelets: 486 [150 - 450] 10^9/L; [redacted]20[redacted] (Rx Day 165): Hemoglobin: 127 [121 - 163] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 164): BLOOD TRANSFUSION 1 UNIT:HB ELEVATED; [redacted]20[redacted] (Rx Day 165): BLOOD TRANSFUSION 1 UNIT:HB ELEVATED TO NORMAL RANGE.

AE Stopped Rx Day	193
Duration of AE	43 DAYS

Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	HAEMMORRHAGIA
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

南アフリカ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，貧血の事象を発現した。

Event 1 の臨床経過：

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

被験者は，20[redacted]年[redacted]月[redacted]日から 20[redacted]年[redacted]月[redacted]日まで先行試験 M16-006 に組み入れられ（被験者番号：[redacted]），盲検化された治験薬が投与された。

投与 151 日後，被験者は貧血を発現した。投与 193 日後，貧血は消失した。

投与 164 日後，被験者は息切れ，倦怠感及び顔面蒼白があったため，入院した。被験者によると，被験者の月経期間は通常 5 日間で，月経期間中輸血が必要になることもあるとのことであった。臨床検査，治療及び輸血が行われた。投与 166 日後，ヘモグロビン値が正常範囲内となり，被験者は退院した。

投与された薬剤は，トラマール，ペチジン，輸血，パントプラゾール，Balsol，ラシックス，鉄剤及び CosmoFer であった。

Causality for RISANKIZUMAB (Blinded)

---

1) Anaemia (10002034) (Anaemia (10002034)) [v.22.1] [10002034]

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 ANAEMIA

- Investigator: Haemmorrhagia

- AbbVie: risk factors include pre-existing anemia and crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD IRON:** 4.0 MCMOL/L (normal 9 to 30.4)

[redacted] **20[redacted] FERRITIN:** 4 ng/mL (normal 13 to 150)

[redacted] **20[redacted] HCT:** 32.8 % (normal 37 to 49)

[redacted] **20[redacted] HEMOGLOBIN:** 9.8 G/DL (normal 12.1 to 16.3)

[redacted] **20[redacted] HEMOGLOBIN:** 12.7 G/DL (normal 12.1 to 16.3)

[redacted] 20[redacted] IRON SATURATION: 5 % (normal 15 to 50)

[redacted] **20[redacted] MCH:** 21.2 PG (normal 27 to 32)

[redacted] **20[redacted] MCHC:** 21.2 G/DL (normal 27 to 32)

[redacted] **20[redacted] PLATELET COUNT:** 486 X10**9/L (normal 150 to 450)

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
ウイルス性胃腸炎	X			X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	5[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
CEREBRAL HEMORRHAGE: CEREBRAL HEMORRHAGE	20[redacted]
CEREBRAL VASCULAR ACCIDENT: CEREBRAL ANEURISM	20[redacted]
CEREBRAL VASCULAR ACCIDENT: CEREBRAL EMBOLISM	20[redacted]
OTHER: PERICARDITIS	20[redacted]
ANEMIA	20[redacted]
OTHER: PERIPHERAL ARTHRITIS	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	30 CIGARETTE	40	
CIGARS	UNKNOWN			
E-CIGARETTES	UNKNOWN			
PIPES	UNKNOWN			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 32	[redacted]20[redacted] / 32	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 63	[redacted]20[redacted] / 63	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 91	[redacted]20[redacted] / 91	1

RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 91 91	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 147 147	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 147 147	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 203 203	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 203 203	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 254 254	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 254 254	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 317 317	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 317 317	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 374 374	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 374 374	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 422 422	1
RISANKIZUMAB	180 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
MESALAZINE	2400 mg	BID	Y-M: 20[redacted] / -92

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	16.6 mg	TID	Y-M: 20[redacted] / 157	ONGOING
METRONIDAZOLE	500 mg	OTHER: X3	Y-M: 20[redacted] / 469	Y-M: 20[redacted] / 469
OMEPRAZOLE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 469	Y-M: 20[redacted] / 469

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

Event Description	VIRAL GASTROENTERITIS
Preferred Term	ウイルス性胃腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 468 (46 DAYS AFTER LAST TREATMENT)

Age at AE Onset 5[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 468): C Reactive Protein: 18.2 [0 - 10] MG/L; NPTST136-COAGULATION: 4441.7 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST477-SARS-COV-2 PCR RINOPHARYNGEAL T: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; [redacted]20[redacted] (Rx Day 470): Albumin: 27 [34 - 49] G/L; Alkaline Phosphatase: 202 [NOT REPORTED - NOT REPORTED] U/L; Amylase: 53 [NOT REPORTED - NOT REPORTED] U/L; Blood Urea Nitrogen: 28 [2.1 - 7.1] MMOL/L; C Reactive Protein: 66.8 [0 - 10] MG/L; Calcium: 2.07 [2.15 - 2.5] MMOL/L; Creatine Kinase: 46 [26 - 192] U/L; Creatinine: 81 [80 - 115] UMOL/L; Erythrocytes: 376 [4.2 - 5.6] 10^12/L; Glucose: 5.1 [4.1 - 5.9] MMOL/L; Hematocrit: 0.37 [0.39 - 0.5] FRACTION OF 1; Hemoglobin: 121 [131 - 172] G/L; Leukocytes: 7760 [4.5 - 11] 10^9/L; NPTST006-?-GT: 10 [NOT REPORTED - NOT REPORTED] U/L; NPTST224-FERRITIN: 11.45 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST318-LDH: 238 [NOT REPORTED - NOT REPORTED] IU/L; NPTST494-SGOT: 13 [NOT REPORTED - NOT REPORTED] U/L; NPTST496-SGPT: 5 [NOT REPORTED - NOT REPORTED] U/L; Phosphate: 0.61 [0.81 - 1.58] MMOL/L; Platelets: 271 [150 - 400] 10^9/L; Potassium: 4.2 [3.5 - 4.5] MMOL/L; Sodium: 143 [136 - 145] MMOL/L; [redacted]20[redacted] (Rx Day 471): NPTST116-CLOSTRIDIUM DIFFICILE: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A

Microbiology

[redacted]20[redacted] (Rx Day 468): OTHER RINOPHARYNGEAL TEST SARS-COV-2 PCR: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 468): CHEST RADIOGRAPHY:NORMAL; [redacted]20[redacted] (Rx Day 472): CT UPPER AND LOWER ABDOMEN:WALL THICKENING OF ILEAL LOOPS AND WALL THICKENING OF SIGMOID COLON AND MESENTERIC LYMPHADENOPATHY, WITHOUT FREE LIQUID.

AE Stopped Rx Day	472 (50 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	VIRAL GASTROENTERITIS
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

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，ウイルス性胃腸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，心膜炎，喫煙者（1 日 30 本を 40 年間）及び飲酒者（1 日 2 杯未満）であった。

投与 468 日後，被験者はウイルス性胃腸炎を発現した。投与 472 日後，ウイルス性胃腸炎は消失した。

投与 468 日後，被験者は発熱（最高 38.8°C）が 8 時間続き，心窩部不快感があったため，入院した。白血球数は増加していた。抗生物質が投与され，被験者の状態は徐々に改善した。投与 472 日後，合併症はなく，被験者は退院した。

投与された薬剤は，Mefoxil，オメプラゾール，シプロフロキサシン及びメトロニダゾールであった。

Causality for RISANKIZUMAB (Blinded)

---

1) Viral gastroenteritis (10047445) (Gastroenteritis viral (10017918)) [v.23.1] [10047445]

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 GASTROENTERITIS

- Investigator: UNDER INVESTIGATION.

- AbbVie: Event common in the general population. Additional risk factor includes pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CHEST RADIOGRAPHY: NORMAL

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 202 U/L

[redacted] 20[redacted] BLOOD UREA NITROGEN: 28 MMOL/L

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

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

[redacted] 20[redacted] CLOSTRIDIUM DIFFICILE: Negative

[redacted] **20[redacted] CT ABDOMEN:** WALL THICKENING OF ILEAL LOOPS AND WALL THICKENING OF SIGMOID COLON AND MESENTERIC LYMPHADENOPATHY, WITHOUT FREE LIQUID.

[redacted] 20[redacted] GLUCOSE: 92 MMOL/L

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 18.2 MG/L

[redacted] 20[redacted] SARS-COV-2 PCR: NEGATIVE

[redacted] 20[redacted] WBC: 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
急性心筋梗塞	X			X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	4[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: TRIGEMINAL NEURALGIA	20[redacted]
OTHER: HUMERUS FRACTURE	20[redacted]
CROHN'S DISEASE	20[redacted]
HYPERLIPIDEMIA: DYSLIPIDEMIA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDICITIS	19[redacted]
SURGERY: TONSILLECTOMY	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	34	
CIGARS	UNKNOWN			
E-CIGARETTES	NEVER			
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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56	1

M16006 /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] / 90	[redacted]20[redacted] / 90	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 147	[redacted]20[redacted] / 147	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 209	[redacted]20[redacted] / 209	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] / 316	[redacted]20[redacted] / 316	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 376	[redacted]20[redacted] / 376	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 428	[redacted]20[redacted] / 428	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
CALCIUM CARBONATE	500 mg	BID	Y-M: 20[redacted] / -83
COLECALCIFEROL	400 IU	BID	Y-M: 20[redacted] / -83

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	400 IU	BID	Y-M: 20[redacted] / -83	ONGOING
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted] / 411	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 411	ONGOING
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 411	ONGOING
EZETIMIBE	10 mg	QD	Y-M: 20[redacted] / 411	ONGOING
METOPROLOL	100 mg	BID	Y-M: 20[redacted] / 411	ONGOING
RAMIPRIL	2,5 mg	QD	Y-M: 20[redacted] / 411	ONGOING
ROSUVASTATIN	10 mg	QD	Y-M: 20[redacted] / 411	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Adjudicated MACE Event, Event of Interest - Adjudicated Extended MACE Event

Event Description	NON ST-ELEVATION MYOCARDIAL INFRACTION

Preferred Term	急性心筋梗塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 411
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 415): Blood Urea Nitrogen: 8.9 [6.4 - 17.8] MMOL/L; Calcium: 2.32 [2.1 - 2.55] MMOL/L; Cholesterol: 137 [NOT REPORTED - 200] mg/dL; Creatinine: 71 [62 - 115] UMOL/L; Glucose: 4.7 [3.9 - 5.6] MMOL/L; Hematocrit: 0.47 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 162 [120 - 160] G/L; NPTST113-CK-MB: 17 [NOT REPORTED - 27] IU/mL; NPTST153-CPK: 121 [NOT REPORTED - 200] U/L; NPTST268-HDL: 40 [40 - NOT REPORTED] mg/dL; NPTST319-LDL: 73 [80 - 130] MG/DL; NPTST333-MAGNESIUM: 2.2 [1.6 - 2.6] MG/DL; NPTST494-SGOT: 43 [5 - 34] U/L; NPTST496-SGPT: 44 [5 - 36] U/L; NPTST532-TROPONIN I: 67.5 [NOT REPORTED - 34.2] ng/mL; NPTST533-TROPONIN T: 26 [NOT REPORTED - 34.2] ng/mL; Platelets: 290 [150 - 450] 10^9/L; Potassium: 4.8 [3.5 - 5] MMOL/L; Prothrombin Intl. Normalized Ratio: 0.9 [0.9 - 1.1] UNIT NOT REPORTED; Sodium: 137 [136 - 145] MMOL/L; Triglycerides: 117 [NOT REPORTED - 150] mg/dL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 412): CORONOGRAPHY & PERCUTANEOUS CORONARY INTERVNTION:CORONARY DISEASE OF ONE SINGLE VESSEL.SUCCESFUL CORONARY ANGIOPLASTY OF LATERAL ANTERIOR DESCENDING ARTERY.; HEART ULTRASOUND:NORMAL DIMENSIONS OF LEFT VENTRICLE AND GOOD CONTRACTION

AE Stopped Rx Day	415
Duration of AE	5 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	HISTORY OF SMOKING
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，非 ST 上昇型心筋梗塞の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，脂質異常症，喫煙者（1 日 1 箱を 34 年間）及び非飲酒者であった。

投与 411 日後，被験者は非 ST 上昇型心筋梗塞を発現した。投与 415 日後，非 ST 上昇型心筋梗塞は消失した。

投与 411 日後，被験者は胸痛のため，入院した。心臓の臨床検査及び診断が行われ，被験者は非 ST 上昇型心筋梗塞を発現したと診断された。投与 412 日後，経皮的冠インターベンション（PCI）による血行再建術が実施された。その結果，1 本の血管の冠疾患が明らかになった。左前下行枝に薬剤溶出ステントが留置された。術後の合併症はなかった。投与 415 日後，被験者は退院した。

投与された薬剤は，Triatec，Salospir，ロスバスタチン亜鉛，エゼチミブ，ロプレソール及びクロピドグレルであった。

The patient's past medications include:

PREZOLON for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Non ST segment elevation myocardial infarction (10064347) (Acute myocardial infarction (10000891)) [v.23.1] [10064347]

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 NON ST-ELEVATION MYOCARDIAL INFRACTION

- **Investigator:** history of smoking

- **AbbVie:** Risk factors include pre-existing dyslipidemia and smoking (1 PPD for 34 years).

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD PRESSURE: 130/80 mmHg

[redacted] 20[redacted] BLOOD UREA NITROGEN: 25 mg/dL (normal 18 to 50)

[redacted] **20[redacted] CALCIUM:** 9.3 mg/dL (normal 8.4 to 10.2)

[redacted] **20[redacted] CHOLESTEROL:** 137 mg/dL (normal <200)

[redacted] **20[redacted] CK-MB:** 17 IU/mL (normal <27)

[redacted] **20[redacted] CPK:** 121 U/L (normal <200)

[redacted] **20[redacted] CREATININE:** 0.8 MG/L (normal 0.7 to 1.3)

[redacted] **20[redacted] ECG:** Normal (sinus rhythm)

[redacted] **20[redacted] GLUCOSE:** 85 mg/dL (normal 70 to 100)

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

[redacted] **20[redacted] HEMATOCRIT:** 47.4 % (normal 37.0 to 47.0)

[redacted] **20[redacted] HEMOGLOBIN:** 16.2 G/DL (normal 12 to 16)

[redacted] **20[redacted] LDL:** 73 mg/dL (normal 80 to 130)

[redacted] **20[redacted] MAGNESIUM:** 2.2 mg/dL (normal 1.6 to 2.6)

[redacted] **20[redacted] PLATELET COUNT:** 290 X10**3/MCL (normal 150 to 450)

[redacted] **20[redacted] POTASSIUM:** 4.8 MEQ/L (normal 3.5 to 5)

[redacted] **20[redacted] SGOT:** 43 U/L (normal 5 to 34)

[redacted] **20[redacted] SGPT:** 44 U/L (normal 5 to 36)

[redacted] **20[redacted] SODIUM:** 137 MEQ/L (normal 136 to 145)

[redacted] **20[redacted] TRIGLYCERIDES:** 117 mg/dL (normal <150)

[redacted] **20[redacted] TROPONIN I:** 67.5 NG/ML (normal <34.2)

[redacted] **20[redacted] TROPONIN T:** 26 NG/ML (normal <34.2)

[redacted] **20[redacted] ULTRASOUND HEART:** Normal dimensions of left ventricle and good contraction.

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
慢性閉塞性肺疾患	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Placebo SC Q8W	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: HYPOTHYROIDISM	19[redacted]
OTHER: DYSTORSION NECK	20
OTHER: RADIAL HEAD FRACTURES LEFT AND RIGHT	20
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE: COPD	20
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE: COPD GOLD II	20
CROHN'S DISEASE	20
OTHER: INTERMITTENT OBSTIPATION	20
OTHER: OBSTIPATION INTERMITTENT	20
PNEUMONIA	20
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE: COPD GOLD III	20
EYE DISEASE/DISORDER: CATARACT LEFT EYE	20
EYE DISEASE/DISORDER: DRY EYES	20
OSTEOPOROSIS	20
OTHER: DYSPNEU	20
OTHER: EXACERBATION COPD (SAE #1)	20
OTHER: POST-MENOPAUSAL	20

Prior Procedures	Procedure Year
SURGERY: SPONDYLODESE (20[redacted]) FOR SPONDYLOLYSE (SINCE 20[redacted])	20
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20
SURGERY: CATARACT RIGHT EYE	20
CROHN'S DISEASE SURGICAL HISTORY: 3X POLYPECTOMY COLON	20
CROHN'S DISEASE HISTORY: COLONOSCOPY	20
CROHN'S DISEASE SURGICAL HISTORY: POLYPECTOMY COLON (3X)	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	7 CIGARETTE	40	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)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 25	[redacted] / 25	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 51	[redacted] / 51	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 88	[redacted] / 88	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 144	[redacted] / 144	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 200	[redacted] / 200	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 261	[redacted] / 261	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted] / 305	[redacted] / 305	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 360	[redacted] / 360	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 417	[redacted] / 417	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ASCORBIC ACID	1000 mg	QD	Y-M: 20[redacted]
MESALAZINE	2 g	PRN	Y-M: 20[redacted]
LEVOTHYROXINE	112,5 mg	QD	Y-M: 20[redacted]
SALBUTAMOL	200 OTHER: UG/DO	PRN	Y-M: 20[redacted]
HYPROMELLOSE	3.2 OTHER: MG/ML	PRN	Y-M: 20[redacted]
LEKOVIT CA	1.25GR/ 800 IE OTHER: GR/IE	QD	Y-M: 20[redacted] / -207
ZOLEDRONIC ACID	5 mg	OTHER: EVERY YEAR ONCE	Y-M: 20[redacted] / -80
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / -61
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -17
AZITHROMYCIN	250 mg	OTHER: 3X/WEEK	Y-M: 20[redacted] / 29
OLODATEROL	5 ug	QD	Y-M: 20[redacted] / 83
TIOTROPIUM	5 ug	QD	Y-M: 20[redacted] / 83

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
MEROKEN NEW	1 OTHER: SACHET	PRN	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 122
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 121	NOT REPORTED
ACETYLCYSTEINE	600 mg	PRN	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 361
IPRATROPIUM	0.5 mg	PRN	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 439
SALBUTAMOL	2.5 mg	PRN	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 439
ALL OTHER NON-THERAPEUTIC PRODUCTS	N/A OTHER: N/A	PRN	Y-M: 20[redacted] / 123	NOT REPORTED
MEROKEN NEW	1 OTHER: SACHET	BID	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 193
ORAL BALANCE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 124
XYLOMETAZOLINE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 147
CODEINE	10 mg	PRN	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 147
MACROGOL	1 OTHER: SACHET	QD	Y-M: 20[redacted] / 202	Y-M: 20[redacted] / 202
MACROGOL	1 OTHER: SACHET	TID	Y-M: 20[redacted] / 203	Y-M: 20[redacted] / 210
MACROGOL	2 OTHER: SACHETS	TID	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 213
MACROGOL	1 OTHER: SACHET	TID	Y-M: 20[redacted] / 214	Y-M: 20[redacted] / 220
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 218	Y-M: 20[redacted] / 234
MACROGOL	1 OTHER: SACHET	BID	Y-M: 20[redacted] / 221	Y-M: 20[redacted] / 254
ERGOCALCIFEROL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 223	Y-M: 20[redacted] / 254
MACROGOL	1 OTHER: SACHET	TID	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 469
COMBIVENT	2.5 mL	QID	Y-M: 20[redacted] / 269	ONGOING
SODIUM CHLORIDE	2.5 mL	BID	Y-M: 20[redacted] / 269	ONGOING
ENEMAS	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 312
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 324	NOT REPORTED

Event #1: Serious Adverse Event

Event Description	EXACERBATION COPD
Preferred Term	慢性閉塞性肺疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 122
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 122): C Reactive Protein: 18 [0 - 10] MG/L; Creatinine: 45 [49 - 90] UMOL/L; NPTST011-ACT.BICARBON.ARTERIAL: 33,4 [22 - 29] mmol/L; NPTST053-BASE EXCESS ARTERIAL: 6.6 [-3 - 3] MMOL/L; NPTST383-O2 SATURATION: 94 [94 - 98] %; NPTST403-PCO2 ARTERIAL: 6.4 [4.3 - 6.4] KPA; NPTST432-PO2 ARTERIAL: 9.6 [11 - 14.4] KPA; [redacted]20[redacted] (Rx Day 123): NPTST011-ACT.BICARBON.ARTERIAL: 34.9 [22 - 29] MMOL/L; NPTST053-BASE EXCESS ARTERIAL: 8.2 [-3 - 3] MMOL/L; NPTST383-O2 SATURATION: 93 [94 - 98] %; NPTST403-PCO2 ARTERIAL: 7.5 [4.3 - 6.4] KPA; NPTST432-PO2 ARTERIAL: 8.3 [11 - 14.4] KPA

Microbiology

[redacted]20[redacted] (Rx Day 122): OTHER THROAT SWAP RESPIRATOIR BANAL CULTURE TEST:; OTHER THROAT SWAP RESPIRATOIR VIRAL QUICK TEST: Negative; URINE URINE BANAL CULTURE TEST: Positive-PSEUDOMONAS AERUGINOSA

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 122): ECG:NORMAL; OXYGEN THERAPY PRN 1-2L:N/A; XTHORAX:NORMAL; [redacted]20[redacted] (Rx Day 123): START WITH POSITIVE EXPIRATORY PRESSURE THERAPY WITH THE AEROBIKA:N/A

AE Stopped Rx Day	129
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PI: COPD GOLD III WORSENING TO EXACERBATION(POSSIBLE VIRAL CAUS). SUBJECT EXPERIENCES EXACERBATIONS MOSTLY WHEN IT'S WINTER
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	EXACERBATION COPD
Preferred Term	慢性閉塞性肺疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 221
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 221): Alkaline Phosphatase: 137 [33 - 98] U/L; C Reactive Protein: 10 [0 - 10] MG/L; Creatinine: 46 [49 - 90] UMOL/L; Eosinophils: 0.62 [0.1 - 0.5] 10^9/L; Eosinophils/Leukocytes: 9.4 [1 - 5] %; Hematocrit: 0.38 [0.35 - 0.45] FRACTION OF 1; Leukocytes: 6.6 [4 - 10] 10^9/L; Monocytes/Leukocytes: 10.8 [2 - 10] %; NPTST018-ALAT: 36 [0 - 34] U/L; NPTST035-ARTERIAL PO2: 8.9 [11 - 14.4] KPA; NPTST203-EPITHELIA: 27 [0 - 10] MCL; NPTST247-GGT: 103 [0 - 40] U/L; NPTST315-LACTATE: 0.4 [0.5 - 1.6] MMOL/L; NPTST403-PCO2 ARTERIAL: 6.2 [4.3 - 6.4] KPA; NPTST505-SQUAMOUS

EPITHELIA: 25 [0 - 10] MCL; NPTST539-UREUM: 2.3 [2.9 - 7.5] MMOL/L; Protein: 40 [0 - 150] MG/L; Sodium: 132 [135 - 145] MMOL/L; Specific Gravity: 1.009 [1.015 - 1.025] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (Rx Day 221): SPUTUM BACTERIAL CULTURE TEST: Positive-1. POLYMORPHNUCL. LEUCOCYTS: SOME 2. PHARYNX EPITHELIAL CELLS: SOME 3. GRAMPOS. COC IN DUPLO: A LOT; OTHER THROAT SWAP COVID-19: Negative; OTHER THROAT SWAP THROAT SWAP: Negative-NEGATIVE FOR: INFLUENZA A VIRUS RNA, INFLUENZA B VIRUS RNA, RSV RNA, METAPNEUMOVIRUS RNA, RHINOVIRUS RNA AND SARS COV RNA; URINE URINE CULTURE: Negative-LEGIONELLE ANTIGEN NEGATIVE, S.PNEUMONIAE ANTIGEN NEGATIVE; [redacted]20[redacted] (Rx Day 222): STOOL COVID-19: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 221): ECG:ABNORMAL NOT CLINICALLY SIGNIFICANT, COMPARABLE WITH PREVIOUS ECG; X-THORAX:NO PULMONARY INFILTATION OR ABNORMALITY VISIBLE

AE Stopped Rx Day	226
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PI: COPD GOLD III WORSENING TO EXACERBATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	EXACERBATION COPD
Preferred Term	慢性閉塞性肺疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 256
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 256): Alkaline Phosphatase: 204 [33 - 98] U/L; C Reactive Protein: 11 [0 - 10] MG/L; NPTST018-ALAT: 55 [0 - 34] U/L; NPTST036-ASAT: 42 [0 - 30] U/L; NPTST183-D-DIMEER: 730 [0 - 630] NG/ML; NPTST204-EPITHELIAL CELLS: 17 [0 - 10] MCL; NPTST247-GGT: 186 [0 - 40] U/L; NPTST383-O2 SATURATION: 93 [94 - 98] %; NPTST432-PO2 ARTERIAL: 8.1 [11 - 14.4] KPA; Sodium: 129 [135 - 145] MMOL/L; [redacted]20[redacted] (Rx Day 257): Sodium: 137 [135 - 145] MMOL/L

Microbiology

[redacted]20[redacted] (Rx Day 256): URINE ANTIGEN TEST: Negative-NEGATIVE FOR LEGIONALLE ANTIGEN AND S.PNEUMONIAE ANTIGEN; SPUTUM BACTERIAL CULTURE TEST: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 256): CT TO RULE OUT LUNG EMBOLISM:NO LUNG EMBOLISMS, CENTRAL BRONCHIUS WALL THICKNING, SOME SMALL AREAS WITH BRONCHIEXTASIS, NO CONSOLIDATIONS, NO SUSPICIOUS INTRAPULMONANARY NODULI; XTHORAX:NO CURRENT PATHOLOGY SEEN

AE Stopped Rx Day	267
Duration of AE	12 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PI: COPD GOLD III WORSENING TO EXACERBATION.

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

Event #4: Serious Adverse Event

Event Description	EXACERBATION COPD
Preferred Term	慢性閉塞性肺疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 321
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 321): Alanine Aminotransferase: 26 [0 - 34] U/L; Alkaline Phosphatase: 71 [33 - 98] U/L; Bilirubin: 5 [0 - 17] UMOL/L; Blood Urea Nitrogen: 3.4 [2.9 - 7.5] MMOL/L; C Reactive Protein: 10 [0 - 10] MG/L; Creatinine: 46 [49 - 90] UMOL/L; Glucose: 6.3 [4 - 7.8] MMOL/L; NPTST009-ACT. BICARBON ART.: 31.4 [22 - 29] MMOL/L; NPTST034-ARTERIAL O2: 8.1 [11 - 14.4] KPA; NPTST053-BASE EXCESS ARTERIAL: 4.9 [-3 - 3] MMOL/L; NPTST247-GGT: 69 [0 - 40] U/L; NPTST383-O2 SATURATION: 92 [94 - 98] %; NPTST403-PCO2 ARTERIAL: 7.3 [4.3 - 6.4] KPA; Potassium: 5 [3.5 - 5] MMOL/L; Sodium: 136 [135 - 145] MMOL/L; [redacted]20[redacted] (Rx Day 324): NPTST010-ACT.,BICARBON. ART: 33.3 [22 - 29] MMOL/L; NPTST052-BASE EXCESS ART.: 7 [-3 - 3] MMOL/L; NPTST403-PCO2 ARTERIAL: 7.1 [4.3 - 6.4] KPA; NPTST432-PO2 ARTERIAL: 8.3 [11 - 14.4] KPA; NPTST480-SATURATION: 92 [94 - 98] %

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 321): ECG:ABNORMAL NOT CLINICALLY SIGNIFICANT, COMPARABLE WITH PREVIOUS ECG; X-THORAX:NO PULMONARY INFILTATION OR ABNORMALITY VISIBLE

AE Stopped Rx Day	326
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PI: COPD GOLD IIII WORSENING TO EXACERBATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #5: Serious Adverse Event

Event Description	EXACERBATION COPD
Preferred Term	慢性閉塞性肺疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 336
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 336): Alanine Aminotransferase: 24 [0 - 34] U/L; Alkaline Phosphatase: 77 [33 - 98] U/L; Bilirubin: 4 [0 - 17] UMOL/L; Blood Urea Nitrogen: 3.8 [2.9 - 7.5] MMOL/L; C Reactive Protein: 10 [0 - 10] MG/L; Creatinine: 54 [49 - 90] UMOL/L; Glucose: 6.6 [4 - 7.8] MMOL/L; NPTST009-ACT. BICARBON ART.: 26.3 [22 - 29] MMOL/L; NPTST034-ARTERIAL O2: 8.5 [11 - 14.4] KPA; NPTST053-BASE EXCESS ARTERIAL: 1 [-3 - 3] MMOL/L; NPTST247-GGT: 92 [0 - 40] U/L; NPTST383-O2 SATURATION: 93 [94 - 98] %; NPTST403-PCO2 ARTERIAL: 5.8 [4.3 - 6.4] KPA; Potassium: 4.6 [3.5 - 5] MMOL/L; Sodium: 139 [135 - 145] MMOL/L; [redacted]20[redacted] (Rx Day 339): NPTST258-GLUCOSE POC: 8.9 [4 - 6.4] MMOL/L; NPTST258-GLUCOSE POC: 4.6 [4 - 6.4] MMOL/L

Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 336): ECG:ABNORMAL NOT CLINICALLY SIGNIFICANT, COMPARABLE WITH PREVIOUS ECG; X-THORAX:NO PULMONARY INFILTATION OR ABNORMALITY VISIBLE

AE Stopped Rx Day	341
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	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

オランダ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，COPD 増悪の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，肺気腫／慢性閉塞性肺疾患，COPD，肺気腫，クローン病，肺炎，COPD 増悪，閉経後症状，元喫煙者（1 日 7 本を 40 年間）及び飲酒者（2 杯未満）であった。

投与 122 日後，被験者は COPD 増悪を発現した。投与 129 日後，COPD 増悪は消失した。

投与 122 日後，被験者は呼吸困難のため入院し，COPD 増悪と診断された。COPD 増悪による呼吸困難のため，必要に応じて 1～2 L の酸素吸入が行われた。高用量コルチコステロイド療法及び酸素療法の後，被験者は徐々に回復した。入院中，被験者の尿中に緑膿菌（非重篤）が検出され，抗生物質によって治療された。投与 129 日後，被験者は退院した。

治験責任医師によると，本事象は COVID-19 とは関連がなかった。

被験者は以前にも（投与の約 1 ヵ月前及び初回投与の翌月）本事象を発現していた。

投与された薬剤は，サルブタモール，イプラトロピウム，酸素及び prednisone であった。Aerobika による呼気陽圧療法も行われた。

Causality for RISANKIZUMAB (Blinded)

---

1) COPD exacerbation (10010953) (Chronic obstructive pulmonary disease (10009033)) [v.23.0] [10010953]

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 COPD

- Investigator: COPD GOLD 3 worsening to exacerbation (possible viral cause). The subject experiences exacerbations mostly when it is winter.

- AbbVie: Reported event more likely related to pre-existing COPD.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BASE EXCESS ARTERIAL: 5.5-6.6 mmol/L

[redacted] **20[redacted] BASE EXCESS ARTERIAL:** 8.2 MMOL/L (normal -3.0 to 3.0)

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

[redacted] **20[redacted] CREATININE:** 45 umol/L (normal 49 to 90)

[redacted] **20[redacted] CRP:** 18 MG/L (normal 0 to 10)

[redacted] 20[redacted] ECG: NORMAL

[redacted] 20[redacted] HCO3 ARTERIAL: 31.6-32.2 mmol/L

[redacted] **20[redacted] HCO3 ARTERIAL:** 34.9 MMOL/L (normal 22.0 to 29.0)

[redacted] 20[redacted] O2 SATURATION: 64-94%

[redacted] **20[redacted] O2 SATURATION:** 93 % (normal 94 to 98)

[redacted] 20[redacted] PCO2 ARTERIAL: 6.4-7.8 KPA

[redacted] **20[redacted] PCO2 ARTERIAL:** 7.5 KPA (normal 4.3 to 6.4)

[redacted] 20[redacted] PO2 ARTERIAL: 4.6-9.6 KPA

[redacted] **20[redacted] PO2 ARTERIAL:** 8.3 KPA (normal 11.0 to 14.4)

[redacted] 20[redacted] RESPIRATOIR BANAL CULTURE TEST: THROAT SWAB: Negative

[redacted] 20[redacted] RESPIRATOIR VIRAL QUICK TEST: Negative

[redacted] 20[redacted] THORAX X-RAY: NORMAL

[redacted] 20[redacted] URINE BANAL CULTURE TEST: Pseudomonas aeruginosa

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 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，COPD 増悪の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，肺気腫／慢性閉塞性肺疾患，肺炎，COPD GOLD III，COPD 増悪，元喫煙者（1 日 7 本を 40 年間）及び飲酒者（1 日 2 杯未満）であった。

投与 221 日後，被験者は COPD 増悪を発現した。投与 226 日後，COPD 増悪は消失した。

投与 221 日後，被験者は COPD 増悪による呼吸困難のため，入院した。高用量コルチコステロイド療法及び酸素吸入が行われた。治療後，呼吸困難は軽減された。投与 226 日後，被験者は退院した。

同定された関連リスク因子は被験者の COPD GOLD III で，呼吸器感染及び増悪のリスクを高めていた。

投与された薬剤は，酸素及び prednisone であった。

The patient's past medications include:

MOVICOLON for OBSTIPATION ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) COPD exacerbation (10010953) (Chronic obstructive pulmonary disease (10009033)) [v.23.0] [10010953]

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 COPD

- Investigator: COPD gold III worsening to exacerbation. Possible COVID-19 infection.- AbbVie: Event more likely related to pre-existing COPD.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ARTERIAL PCO2:** 6.2 KPA (normal 4.3 to 6.4)

[redacted] **BACTERIAL CULTURE:** 1. POLYMORPHNUCL. LEUCOCYTS: SOME 2. PHARYNX EPITHELIAL CELLS: SOME 3. GRAM POS. COC IN DUPLO: A LOT

[redacted] COVID-19 TEST: Throat swap: Negative

[redacted] **COVID-19 TEST:** Stool sample: Negative

[redacted] CRP: <10 mg/L

[redacted] **ECG:** Abnormal not clinically significant, comparable with previous ECG

[redacted] **LACTATE:** 0.4 MMOL/L (normal 0.5 to 1.6)

[redacted] **SPUTUM CULTURE:** 1. POLYMORPHNUCL. LEUCOCYTS: SOME 2. PHARYNX EPITHELIAL CELLS: SOME 3. GRAMPOS. COC IN DUPLO: A LOT

[redacted] **20[redacted] THORAX X-RAY:** No pulmonary infiltration or abnormality visible

[redacted] **20[redacted] THROAT SWAB:** NEGATIVE FOR: INFLUENZA A VIRUS RNA, INFLUENZA B VIRUS RNA, RSV RNA, METAPNEUMOVIRUS RNA, RHINOVIRUS RNA AND SARS COV RNA

[redacted] **20[redacted] WBC:** 6.62.3 X10**9/L (normal 4.0 to 10.0)

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，COPD 増悪の事象を発現した。

Event 3 の臨床経過：

関連する病歴は，甲状腺機能低下症，肺気腫／慢性閉塞性肺疾患，クローン病，肺炎，COPD GOLD III，呼吸困難，COPD 増悪，元喫煙者（1 日 7 本を 40 年間，20[redacted] 年に禁煙）及びアルコール摂取（1 日 2 杯未満）であった。

投与 256 日後，被験者は COPD 増悪を発現した。投与 267 日後，COPD 増悪は消失した。

投与 256 日後，被験者は COPD 増悪による重度の呼吸困難のため，来院した。高用量コルチコステロイド療法，酸素療法及び臨床検査が行われた。呼吸困難は軽減され，被験者の状態は改善した。投与 261 日後，被験者は退院した。

治験責任医師は，COPD Gold III のため，被験者は呼吸器感染及び増悪のリスクが高いことを指摘した。

投与された薬剤は，Fluimucil（アセチルシステイン）及び prednisone であった。

Causality for RISANKIZUMAB (Blinded)

---

1) COPD exacerbation (10010953) (Chronic obstructive pulmonary disease (10009033)) [v.23.0] [10010953]

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 COPD

- Investigator: PI: COPD GOLD III WORSENING TO EXACERBATION.

-AbbVie: Event more likely related to pre-existing Emphysema/Chronic Obstructive Pulmonary Disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALK PHOS:** 204 U/L (normal 33 to 98)

[redacted] **20[redacted] ALT:** 55 U/L (normal 0 to 34)

[redacted] **20[redacted] ANTIGEN TEST:** Negative: NEGATIVE FOR LEGIONALLE ANTIGEN AND S.PNEUMONIAE ANTIGEN

[redacted] **20[redacted] ARTERIAL PO2:** 8.1 KPA (normal 11 to 14.4)

[redacted] **20[redacted] AST:** 42 U/L (normal 0 to 30)

[redacted] 20[redacted] BACTERIAL CULTURE TEST: Not reported

[redacted] **20[redacted] CHEST X-RAY:** NO CURRENT PATHOLOGY SEEN

[redacted] 20[redacted] COVID-19 TEST: NEGATIVE

[redacted] **20[redacted] CT:** NO LUNG EMBOLISM, CENTRAL BRONCHIUS WALL THICKNING, SOME SMALL AREAS WITH BRONCHIEXTASIS, NO CONSOLIDATIONS, NO SUSPICIOUS INTRAPULMONANARY NODULI

[redacted] **20[redacted] D-DIMER:** 730 NG/ML (normal 0 to 630)

[redacted] 20[redacted] EPITHELIAL CELLS: 17 MCL (normal 0 to 10)

[redacted] **20[redacted] GGT:** 186 U/L (normal 0 to 40)

[redacted] 20[redacted] HIGH-SENSITIVE C REACTIVE PROTEIN: 11 MG/L (normal 0 to 10)

[redacted] **20[redacted] O2 SATURATION:** 93 % (normal 94 to 98)

[redacted] **20[redacted] SODIUM:** 129 MMOL/L (normal 135 to 145)

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

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及びリサンキズマブが投与され，COPD 増悪の事象を発現した。

Event 4 の臨床経過：

関連する病歴は，肺気腫／慢性閉塞性肺疾患，肺気腫／慢性閉塞性肺疾患（COPD GOLD II），クローン病，肺炎，肺気腫／慢性閉塞性肺疾患（COPD GOLD III），COPD 増悪，閉経後症状，元喫煙者（1 日 7 本を 40 年間）及び現飲酒者（1 日 2 杯未満）であった。

投与 305 日後，非盲検化されたリサンキズマブによるレスキュー治療が開始された。本事象発現時，被験者は 360 mg 皮下注射（非盲検）療法の初回投与を受けていなかった。

投与 321 日後，被験者は COPD 増悪を発現した。投与 326 日後，COPD 増悪は消失した。

本事象発現前の投与の約 1 ヵ月前（先行試験中），投与 122 日後（AER # [redacted]），投与 188 日後（非重篤），投与 221 日後（AER # [redacted]），投与 256 日後（AER # [redacted]）及び投与 281 日後（非重篤），被験者は COPD 増悪を発現した。

投与 321 日後，被験者は COPD 増悪による呼吸困難のため，入院した。高用量コルチコステロイド療法，抗生物質の投与及び酸素療法が行われた。呼吸困難は軽減され，被験者の状態は改善した。投与 326 日後，被験者は退院した。

投与された薬剤は，酸素，prednisone 及びアジスロマイシンであった。

Causality for RISANKIZUMAB (Blinded)

---

1) COPD exacerbation (10010953) (Chronic obstructive pulmonary disease (10009033)) [v.23.0] [10010953]

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) COPD exacerbation (10010953) (Chronic obstructive pulmonary disease (10009033)) [v.23.0] [10010953]

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 COPD

- Investigator: PI: COPD Gold III worsening to exacerbation.

- AbbVie: event is more likely related to pre-existing history of emphysema/ chronic obstructive pulmonary disease.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of EXACERBATION COPD

- Investigator: PI: COPD Gold III worsening to exacerbation.

- AbbVie: event is more likely related to pre-existing history of emphysema/ chronic obstructive pulmonary disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BASE EXCESS ARTERIAL:** 4.9 MMOL/L (normal -3.0 to 3.0)

[redacted] **BASE EXCESS ARTERIAL:** 7.0 MMOL/L (normal -3.0 to 3.0)

[redacted] **BICARBONATE ARTERIAL:** 31.4 MMOL/L (normal 22.0 to 29.0)

[redacted] **20[redacted] BICARBONATE ARTERIAL:** 33.3 MMOL/L (normal 22.0 to 29.0)

[redacted] 20[redacted] CRP: <10 mg/L

[redacted] **20[redacted] ECG:** Abnormal not clinically significant, comparable with previous ECG.

[redacted] **20[redacted] GGT:** 69 U/L (normal 0 to 40)

[redacted] **20[redacted] O2 SATURATION:** 92 % (normal 94 to 98)

[redacted] **20[redacted] O2 SATURATION:** 92 % (normal 94 to 98)

[redacted] **20[redacted] PCO2 ARTERIAL:** 7.3 KPA (normal 4.3 to 6.4)

[redacted] **20[redacted] PCO2 ARTERIAL:** 7.1 KPA (normal 4.3 to 6.4)

[redacted] **20[redacted] PO2 ARTERIAL:** 8.1 KPA (normal 11.0 to 14.4)

[redacted] **20[redacted] PO2 ARTERIAL:** 8.3 KPA (normal 11.0 to 14.4)

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

[redacted] **20[redacted] X-THORAX:** No pulmonary infiltration or abnormality visible.

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及びリサンキズマブが投与され，COPD 増悪の事象を発現した。

Event 5 の臨床経過：

関連する病歴は，甲状腺機能低下症，脊椎固定，COPD，COPD GOLD II，クローン病，肺炎，COPD GOLD III，元喫煙者（1 日 7 本を 40 年間），呼吸困難，飲酒者（1 日 2 杯未満）及び脊椎分離であった。

20[redacted] 年 [redacted] 月 [redacted] 日，非盲検化されたリサンキズマブによるレスキュー治療が開始された。本事象発現時，被験者は 360 mg 皮下注射（非盲検）療法の初回投与を受けていなかった。

投与 336 日後，被験者は COPD 増悪を発現した。投与 341 日後，COPD 増悪は消失した。

本事象発現前の投与の約 1 ヵ月前（先行治験中），投与 122 日後（AER # [redacted]），投与 221 日後（AER # [redacted]），投与 256 日後（AER # [redacted]

[redacted]）及び投与 321 日後（AER # [redacted]），被験者は COPD 増悪を発現した。

投与 336 日後，被験者は，呼吸困難の主訴で入院した。高用量ステロイド療法及び酸素療法が行われた。投与 341 日後，被験者は退院した。

治験責任医師によると，被験者は Gold III COPD の既往によって呼吸器感染及び増悪のリスク因子が高くなっている。

投与された薬剤は，prednisone，アジスロマイシン及びスピオルトであった。

Causality for RISANKIZUMAB (Blinded)

---

1) COPD exacerbation (10010953) (Chronic obstructive pulmonary disease (10009033)) [v.23.0] [10010953]

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) COPD exacerbation (10010953) (Chronic obstructive pulmonary disease (10009033)) [v.23.0] [10010953]

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 COPD

- Investigator: Exacerbation.

- AbbVie: Event is more likely related to pre-existing history of emphysema/ chronic obstructive pulmonary disease.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of EXACERBATION COPD

- Investigator: Exacerbation

- AbbVie: Event is more likely related to pre-existing history of emphysema/ chronic obstructive pulmonary disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ARTERIAL BASE EXCESS: 1 MMOL/L (normal -3 to 3)

[redacted] **20[redacted] ARTERIAL BICARBONATE:** 26.3 MMOL/L (normal 22 to 29)

[redacted] **20[redacted] ARTERIAL O2:** 8.5 KPA (normal 11 to 14.4)

[redacted] 20[redacted] ARTERIAL O2 SATURATION: 93 % (normal 94 to 98)

[redacted] **20[redacted] ARTERIAL PCO2:** 5.8 KPA (normal 4.3 to 6.4)

[redacted] **20[redacted] CHEST XRAY:** NO PULMONARY INFILTATION OR ABNORMALITY VISIBLE

[redacted] 20[redacted] COVID-19 TEST: Tested negative

[redacted] **20[redacted] ECG:** ABNORMAL NOT CLINICALLY SIGNIFICANT, COMPARABLE WITH PREVIOUS ECG

[redacted] **20[redacted] POC GLUCOSE:** 8.9 MMOL/L (normal 4 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
肛門膿瘍	X			X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: HEADACHE	19[redacted]
CROHN'S DISEASE	19
OTHER: ANAL PAIN	20
OTHER: DRY SKIN	20
OTHER: NAEVI WHOLE BODY	20
OTHER: ACUTE PERFORATION IN SMALL INTESTINE	20
OTHER: FATIGUE	20
OTHER: STENOSIS TRANSITION JEJENUM-ILEUM	20
ANEMIA: IRON DEFICIENCY ANEMIA	20
OSTEOARTHRITIS	20
OTHER: MULTINODULAR WITH THYROID BLOOD CYSTE RIGHT	20
OTHER: PYROSIS	20
OTHER: ANAL FISSURE	20
OTHER: ANAL INFECTION DRAINING PUS	20
OTHER: ANAL FISSURE	20
OTHER: FACIAL HAIR GROWTH	20
CHOLECYSTITIS	20
OTHER: CHOLEDOCHOLITHIASIS	20
OTHER: PALE FACE	20
OTHER: VIT D DEFICIENCY	20
OTHER: VOMITING	20
OTHER: MUSCLE PAIN	20
OTHER: OEDEMA LEGS	20
OTHER: RHINITIS WITH CRUSTAE	20
EYE DISEASE/DISORDER: BLEFARITIS	20
OTHER: RIGHT HEMITHYROIDECTOMIE	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: HEMICOLECTOMY	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20
SURGERY: CHOLEDOCYSTECTOMIE	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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 24	[redacted] / 24	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 52	[redacted] / 52	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 93	[redacted] / 93	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 93	[redacted] / 93	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 120	[redacted] / 120	1
M16006 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 143	[redacted] / 143	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 143	[redacted] / 143	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 167	[redacted] / 167	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 219	[redacted] / 219	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 275	[redacted] / 275	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 335	[redacted] / 335	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted] / 344	[redacted] / 344	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 393	[redacted] / 393	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 451	[redacted] / 451	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 506	[redacted] / 506	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
NEUROBION	1 OTHER: AMPULE	OTHER: EVERY 3 MONTH	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: ONCE	Y-M: 20[redacted]
ADALIMUMAB	160 mg	OTHER: ONCE	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: ONCE	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: ONCE	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	Q2M	Y-M: 20[redacted] / -364
VEDOLIZUMAB	300 mg	Q2M	Y-M: 20[redacted] / -309
NUVARING	12 mg	QD	Y-M: 20[redacted] / -110
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / -77

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] / 200	Y-M: 20[redacted] / 450

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

Event Description ANAL ABSCESS WITH EXTENSION ABOVE THE ELEVATOR MUSCLES

Preferred Term 肛門膿瘍

AE Onset Date / Rx Day [redacted]20[redacted] / 315

Age at AE Onset 3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 314): C Reactive Protein: 100 [0 - 7] MG/L; [redacted]20[redacted] (Rx Day 322): C Reactive Protein: 6.1 [0 - 7] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 285): INCISION AND DRAINAGE:RESOLVED; [redacted]20[redacted] (Rx Day 312): TEMPERATURE:38.9?C; [redacted]20[redacted] (Rx Day 313): TEMPERATURE:39.2?C; [redacted]20[redacted] (Rx Day 314): TEMPERATURE:37.8?C; [redacted]20[redacted] (Rx Day 315): MRI PELVIS:ANAL ABSCESS

AE Stopped Rx Day	323
Duration of AE	9 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN'S DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	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，肛門挙筋上に進展した肛門膿瘍の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，肛門痛，小腸の急性穿孔，半結腸切除，空腸-回腸移行部狭窄，変形性関節症，裂肛，肛門感染排膿，裂肛，結腸内視鏡検査，非喫煙者及び非飲酒者であった。

投与 315 日後，被験者は肛門挙筋上に進展した肛門膿瘍を発現した。投与 323 日後，肛門挙筋上に進展した肛門膿瘍は消失した。

投与 316 日後，被験者は間欠熱及び肛門膿排出のため入院した。投与 316 日後，肛門切開及び排膿が行われ，被験者の臨床経過は良好であった。投与 317 日後，被験者は退院した。

投与された薬剤は，Amoxiclav 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])

VEDOLIZUMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Anal abscess (10048946) (Anal abscess (10048946)) [v.22.1] [10048946]

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 ANAL ABSCESS WITH EXTENSION ABOVE THE ELEVATOR MUSCLES

- **Investigator:** Crohn's disease.

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

Relevant Laboratory & Other Diagnostic Tests

Unknown date CRP: 100 MG/L

[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 100 KU/L (normal 0.0 to 7.0)

[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 6.1 MG/L (normal 0.00 to 7.0)

[redacted] MRI PELVIS: ANAL ABSCESS

[redacted] TEMPERATURE: 38.9°C

[redacted] TEMPERATURE: 39.2°C

[redacted] TEMPERATURE: 37.8°C

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			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: EROSIVE BULBITIS DUE TO HELICOBACTER PYLORIS POSITIVE	19[redacted]
CROHN'S DISEASE	19
OTHER: FATIGUE	19
OTHER: HEADACHE	19
OSTEOARTHRITIS: LOW BACK PAIN AND JOINT PAIN	20
OTHER: LOW BACK PAIN	20
OTHER: SLEEPING PROBLEMS	20
OTHER: RECURRENT OBSTRUCTION	20
OTHER: MENOPAUZAL	20

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

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	20 CIGARETTE	45	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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1

M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20 / 33	[redacted]20 / 33	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20 / 33	[redacted]20 / 33	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20 / 61	[redacted]20 / 61	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20 / 61	[redacted]20 / 61	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 89	[redacted]20 / 89	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 89	[redacted]20 / 89	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 147	[redacted]20 / 147	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 147	[redacted]20 / 147	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 203	[redacted]20 / 203	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 203	[redacted]20 / 203	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20 / 225	[redacted]20 / 225	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 257	[redacted]20 / 257	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 313	[redacted]20 / 313	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 376	[redacted]20 / 376	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / 427	[redacted]20 / 427	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
PARACETAMOL	1 g	PRN	Y-M: 19[redacted]
INFLIXIMAB	5 mg/kg	OTHER: ONCE	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	QM	Y-M: 20[redacted]
LORAZEPAM	1.25 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	QM	Y-M: 20[redacted]
CERTOLIZUMAB	400 mg	OTHER: ONCE	Y-M: 20[redacted]
CERTOLIZUMAB	400 mg	OTHER: ONCE	Y-M: 20[redacted]
CERTOLIZUMAB	400 mg/kg	OTHER: ONCE	Y-M: 20[redacted]
CERTOLIZUMAB	400 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
FOLIC ACID	4 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: ONCE	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	160 mg	OTHER: ONCE	Y-M: 20[redacted]

ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	Q2M	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	QM	Y-M: 20[redacted]
NEUROBION	3 mL	OTHER: EVERY 3 MONTH	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
NOT REPORTED				

Event #1: Serious Adverse Event

Event Description	BOWEL OBSTRUCTION (PRETERMINAL ILEUM)
Preferred Term	小腸閉塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 114
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 114): CT ABDOMEN:DISTENTION OF SEVERAL JEJUNAL SMALL INTESTINAL DECAYS TO THE LEVEL IN THE SMALL PELVIS ON THE RIGHT. WE SEE PRESENCE OF A ZONE OF 8 CM WITH A CLEARLY THICKENED INTESTINAL WALL. THE PRETERMINAL ILEUM.

AE Stopped Rx Day	117
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN'S DISEASE RELATED
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，腸閉塞（回腸末端前）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，ヘリコバクター・ピロリ陽性によるびらん性十二指腸球炎，クローン病，再発性消化管閉塞，腸切除，元喫煙者（1日20本を45年間）及びアルコール摂取（1日2杯未満）であった。

投与114日後，被験者は腸閉塞（回腸末端前）を発現した。投与117日後，腸閉塞（回腸末端前）は消失した。

投与114日後，被験者は悪心，嘔吐，腹痛及び悪寒のため，入院した。被験者は亜閉塞の臨床像があり，入院した。被験者の症状は，以前の発現時と類似していた。被験者は投与の約13年前，投与の約17ヵ月前及び投与の約8ヵ月前に同様の事象を発現していた。

同日，腹部CTスキャン検査で小骨盤腔右側に空腸内腐敗物による膨満が認められた。腸管壁が明らかに肥厚した8 cmの領域が回腸末端部より前の位置に認められた。

絶食及び静脈内補液による保存的治療が行われた。主訴は自然に改善した。経口摂取は徐々に再開された。投与117日後，被験者は退院した。

投与された薬剤は，Tiorfix，ブスコパン及びクレキサンであった。

Causality for RISANKIZUMAB (Blinded)

---

1) Ileal obstruction (10065730) (Small intestinal obstruction (10041101)) [v.21.1] [10065730]

Causalitys 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 BOWEL OBSTRUCTION (PRETERMINAL ILEUM)

- Investigator: CROHN'S DISEASE RELATED

- AbbVie: RISK FACTOR INCLUDES PRE-EXISTING CROHN'S DISEASE

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN:** DISTENTION OF SEVERAL JEJUNAL SMALL INTESTINAL DECAYS TO THE LEVEL IN THE SMALL PELVIS ON THE RIGHT. WE SEE PRESENCE OF A ZONE OF 8 CM WITH A CLEARLY THICKENED INTESTINAL WALL. THE PRETERMINAL ILEUM. THE IMAGE MAY INDICATE OBSTRUCTION TO POSSIBLE INFLAMMATION AND LESS LIKELY TUMOR OF THE PRETERMINAL ILEUM. THE IMAGE MAY INDICATE A FLARE OF CROHN'S. AROUND THIS INTESTINAL LOOP IS A SMALL INFILTRATION. WE SEE PRESENCE OF SOME SMALL MESENTERIC GLANDS. NO INTRA-ABDOMINAL FREE FLUID. NO ENCAPSULATED COLLECTIONS INTRA-ABDOMINAL. NO DETACHABLE PERFORATION.

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
虫垂炎	X			X

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	2[redacted]	MALE	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	FORMER	4 CIGARETTE	6	20[redacted]
CIGARS	FORMER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 37	[redacted]20[redacted] / 37	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 58	[redacted]20[redacted] / 58	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] / 148	[redacted]20[redacted] / 148	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 148	[redacted]20[redacted] / 148	1

PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 205	[redacted]20[redacted] / 205	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 205	[redacted]20[redacted] / 205	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 260	[redacted]20[redacted] / 260	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 260	[redacted]20[redacted] / 260	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 328	[redacted]20[redacted] / 328	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 328	[redacted]20[redacted] / 328	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 373	[redacted]20[redacted] / 373	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 373	[redacted]20[redacted] / 373	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 436	[redacted]20[redacted] / 436	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 436	[redacted]20[redacted] / 436	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ADALIMUMAB	160 mg	OTHER: ONCE	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: ONCE	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: ONCE	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	QM	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: ONCE	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	10 mg/kg	OTHER: ONCE	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	Q2M	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted] / -202

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: ONCE	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 236
PARACETAMOL	1 g	OTHER: ONCE	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 237
DICLOFENAC	75 mg	BID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 243

PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 243
PARACETAMOL	1 g	OTHER: 4 TIMES A DAY	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 243
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 243

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

Event Description	ACUTE APPENDICITIS
Preferred Term	虫垂炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 235
Age at AE Onset	2[redacted]
Laboratory Testing	[redacted]20[redacted] (Rx Day 236): NPTST160-CRP: 86 [0 - 5] MG/L; [redacted]20[redacted] (Rx Day 238): C Reactive Protein: 111 [0 - 5] MG/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (Rx Day 236): ABDOMINAL ULTRASOUND:RESULT OF ACUTE APPENDICITIS, WITHOUT SIGN OF PERFORATION; [redacted]20[redacted] (Rx Day 237): APPENDECTOMY:ACUTE APPENDICIT TREATED DUE TO APPENDECTOMY
AE Stopped Rx Day	237
Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NO REASONABLE POSSIBILITY, INFECTION OF THE APPENDIX CAN HAPPEN TO ANYONE, NO PREDISPOSITION
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，急性虫垂炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元喫煙者（1 日 4 箱を 6 年間），クローン病及び現飲酒者（1 日 2 杯未満）であった。

投与 235 日後，被験者は急性虫垂炎を発現した。投与 237 日後，急性虫垂炎は消失した。

投与 236 日後，被験者は下腹部痛の主訴で入院した。CRP は 86 であった。腹部検査が行われ，マックバーニー圧痛点陽性により虫垂炎が示唆された。腹部超音波検査で虫垂炎が確認された。投与 237 日後，腹腔鏡下虫垂切除が行われた。術後合併症はなく，オーグメンチン投与下で臨床的及び生化学的経過は良好であった。被験者は退院した。

投与された薬剤は，Augmentin Retard，paracetamol，Pantomed，Paracetabs Forte，Tradonal Odis，Dafalgan 及びジクロフェナクであった。

The patient's past medications include:

VEDOLIZUMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Acute appendicitis (10000677) (Appendicitis (10003011)) [v.22.0] [10000677]

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 APPENDICITIS

- Investigator: No reasonable possibility, infection of the appendix can happen to anyone, no predisposition

- AbbVie: Event is a common complication. Appendicitis is seen in up to 1 in 10 individuals over a lifetime. (acute appendicitis in adults: diagnostic evaluation. In: up to date, post tw (ed) , up to date, waltham, ma. (accessed on [redacted])

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL ULTRASOUND: Appendicitis confirmed.

[redacted] **20[redacted] CRP:** 86 MG/L (normal 0 to 5)

[redacted] **20[redacted] MCBURNEY TEST:** Positive - acute appendicitis

[redacted] **20[redacted] PATHOLOGY:** acute appendicitis with peri-appendicitis

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
腹膜障害	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: MICROCYTAIRE ANEMIA	NOT REPORTED
OSTEOARTHRITIS	NOT REPORTED
OTHER: ALLERGY TO GRASS AND BIRCH	NOT REPORTED
OTHER: CACHEXIE	NOT REPORTED
CROHN'S DISEASE	20[redacted]
CARDIAC ARRHYTHMIA: PAROXYSTIQUE FIBRILATION AURICULAIRE	20
OTHER: PNEUMOPATIE - BOOP	20
EYE DISEASE/DISORDER: EPISCLERITIS	20
OTHER: ERYTHEMA NODOSUM	20
OTHER: FISTULE RECTO VAGINALE	20
OTHER: PLEUROPERICARDITIS	20
MIGRAINE HEADACHE	20
CARDIAC ARRHYTHMIA: EXTRASYSTOLE SUPRAVENTRICULAIRE	20
OTHER: VITAMINE D DEFICICENCY	20

Prior Procedures	Procedure Year
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: PLACEMENTS OF SETONS	20
CROHN'S DISEASE SURGICAL HISTORY: PLACEMENT OF TOTAL PARENTERAL NUTRITION	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)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 29	[redacted] / 29	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 63	[redacted] / 63	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 82	[redacted] / 82	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 82	[redacted] / 82	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 133	[redacted] / 133	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 133	[redacted] / 133	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 193	[redacted] / 193	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 193	[redacted] / 193	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 252	[redacted] / 252	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 252	[redacted] / 252	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 302	[redacted] / 302	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 302	[redacted] / 302	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 365	[redacted] / 365	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 365	[redacted] / 365	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 421	[redacted] / 421	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 421	[redacted] / 421	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
PARACETAMOL	1 g	PRN	Y-M: 20[redacted]
INFLIXIMAB	UNK mg/kg	Q2M	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	NOT APPLICABLE OTHER: NOT APPLICABLE	OTHER: NOT APPLICABLE	Y-M: 20[redacted] / -295

ADALIMUMAB	80 mg	OTHER: ONCE	Y-M: 20[redacted] / -255
ADALIMUMAB	160 mg	OTHER: ONCE	Y-M: 20[redacted] / -247
ADALIMUMAB	40 mg	OTHER: EVERY 2 WEEKS	Y-M: 20[redacted] / -224
ADALIMUMAB	40 mg	OTHER: ONCE A WEEK	Y-M: 20[redacted] / -194
LEKOVIT CA	1 OTHER: TAB	QD	Y-M: 20[redacted] / -194
FOLIC ACID	4 mg	QD	Y-M: 20[redacted] / -50
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / -38
MESALAZINE	3 g	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
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 133
LEKOVIT CA	1 OTHER: TAB	QD	Y-M: 20[redacted] / -194	Y-M: 20[redacted] / 133
IRON	1 g	OTHER: ONCE	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 87

Event #1: Serious Adverse Event

Event Description	PERITONEALE SYNDROM
Preferred Term	腹膜障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 82
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 85): NPTST160-CRP: 88.7 [NOT REPORTED - 5] mg/L; [redacted]20[redacted] (Rx Day 86): NPTST160-CRP: 38.8 [NOT REPORTED - 5] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 83): ABDOMINAL SCANNER:NO SIGNS OF COMPLICATION

AE Stopped Rx Day	87
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	COLONOSCOPY ASKING BY PROTOCOLE TO CHECK THE CROHN 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

ベルギー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，腹膜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，穿通型），不整脈（発作性心房細動），肺疾患（BOOP），胸膜心膜炎，不整脈（期外収縮上室性頻拍），シートン留置，中心静脈カテーテル留置，悪液質，非喫煙者及び非飲酒者であった。

投与 82 日後，被験者は腹膜障害を発現した。投与 87 日後，腹膜障害は消失した。

投与 82 日後，被験者は結腸内視鏡検査を受けた。被験者によると，投与 82 日後の夕方から腹痛があり，paracetamol を服用したが，痛みは軽減しなかったとのことであった。投与 83 日後，結腸内視鏡検査の合併症を評価するため，被験者は入院した。腹部スキャン検査を実施したが，合併症は認められなかった。抗生物質が投与された。投与 87 日後，被験者は良好な状態で退院した。

投与された薬剤は，Ciproxine，フラジール，メトロニダゾール，paracetamol 及び Zinacef 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], [redacted]20[redacted] - [redacted]20[redacted], [redacted]20[redacted] - [redacted]20[redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Peritoneal disorder (10061343) (Peritoneal disorder (10061343)) [v.23.1] [10061343]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of PERITONEALE SYNDROM

- Investigator: Colonoscopy asking by protocole to check the Crohn's disease.

- AbbVie: Event more likely related to complications after colonoscopy. Additional risk factor includes pre-existing Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMEN ULTRASOUND: No signs of complication.

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
疼痛	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	19[redacted]
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	19
OTHER: ARTHRALGIA (INTERMITTENT)	19
OTHER: HEADACHE	20
OTHER: OBESITY	20
OTHER: TINEA PEDIS	20
OTHER: PATELLA FRACTURE	20
CHOLELITHIASIS	20
OTHER: GASTRITIS	20
HYPERTENSION	20
OTHER: INSOMNIA	20
OTHER: ELEVATED GAMMA GT BLOOD VALUE	20
OTHER: CAMPYLOBACTER JEJUNI INFECTION	20
GASTROESOPHAGEAL REFLUX DISEASE	20
OTHER: MUSCLE CRAMPS	20

Prior Procedures	Procedure Year
SURGERY: MENISCUS SURGERY	19[redacted]
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	19
SURGERY: FISTULOTOMY	19
SURGERY: SECTIO CAESAREA	20
SURGERY: SECTIO CAESAREA	20
SURGERY: CHOLECYSTECTOMY	20
CROHN'S DISEASE HISTORY: COLONOSCOPY	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	25 CIGARETTE	22	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 29	[redacted] / 29	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 62	[redacted] / 62	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 91	[redacted] / 91	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 91	[redacted] / 91	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 147	[redacted] / 147	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 147	[redacted] / 147	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 205	[redacted] / 205	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 205	[redacted] / 205	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 258	[redacted] / 258	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 258	[redacted] / 258	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 314	[redacted] / 314	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 314	[redacted] / 314	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 370	[redacted] / 370	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 370	[redacted] / 370	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 428	[redacted] / 428	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted] / 428	[redacted] / 428	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
PARACETAMOL	1 g	PRN	Y-M: 19[redacted]
BISOPROLOL	5 mg	QD	Y-M: 20[redacted]
DIAZEPAM	10 mg	PRN	Y-M: 20[redacted]

TRAZODONE	100 mg	QD	Y-M: 20[redacted]
PANTOPRAZOLE	20 mg	PRN	Y-M: 20[redacted]
D-VITAL CALCIUM	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -34
CALCIUM LEVOMEFOLATE W/CYANOCOBALAMIN/MAGNESI	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / -23
HYOSCINE	10 mg	PRN	Y-M: 20[redacted] / -23
RENNIE	760 mg	PRN	Y-M: 20[redacted] / -23
EUGYNON	0.12 mg	QD	Y-M: 20[redacted] / 8
CYANOCOBALAMIN	1 mg	OTHER: 1/3MONTHS	Y-M: 20[redacted] / 28

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
PARACETAMOL	1 g	PRN	Y-M: 19[redacted]	NOT REPORTED
BISOPROLOL	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
DIAZEPAM	10 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
TRAZODONE	100 mg	QD	Y-M: 20[redacted]	NOT REPORTED
PANTOPRAZOLE	20 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
CALCIUM LEVOMEFOLATE W/CYANOCOBALAMIN/MAGNESI	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / -23	NOT REPORTED
HYOSCINE	10 mg	PRN	Y-M: 20[redacted] / -23	NOT REPORTED
RENNIE	760 mg	PRN	Y-M: 20[redacted] / -23	NOT REPORTED
CYANOCOBALAMIN	1 mg	OTHER: 1/3MONTHS	Y-M: 20[redacted] / 28	NOT REPORTED
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted] / 94	Y-M: 20[redacted] / 221
TRAMADOL	100 mg	BID	Y-M: 20[redacted] / 154	NOT REPORTED
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 154	NOT REPORTED
EUGYNON	0.18 mg	QD	Y-M: 20[redacted] / 163	NOT REPORTED
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 222	Y-M: 20[redacted] / 252
GADOBENIC ACID	15 mL	QD	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 241
SODIUM CHLORIDE	10 mL	QD	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 241

ANTIFUNGALS FOR TOPICAL USE	NOT REPORTED	BID	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 255

Event #1: Serious Adverse Event

Event Description	CHRONIC PAIN SYNDROME
Preferred Term	疼痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 239
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx Day 240): X-RAY THORAX:NORMAL; [redacted]20[redacted] (Rx Day 241): MR LIVER:FOCAL NODULAR HYPERPLASIA IN LIVER; ULTRA SOUND LEFT SHOULDER:CALCIFICATION SUPRASPINATUS TENDON; ULTRASOUND ABDOMEN:SHOWED ISOREFLECTIVE LESION IN LIVER FOR WHICH MRI; X-RAY LEFT SHOULDER:ACROMION TYPE 2; X-RAY PLEVIS:NORMAL; [redacted]20[redacted] (Rx Day 245): ELECTROMYOGRAPHY:NORMAL	
AE Stopped Rx Day	245
Duration of AE	7 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	OBESITY
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，慢性疼痛症候群の事象を発現した。

Event 1 の臨床経過：

投与 239 日後，被験者は慢性疼痛症候群を発現した。投与 245 日後，慢性疼痛症候群は消失した。

投与 239 日後，被験者は入院した。被験者によると，被験者は投与から約 5 ヵ月後から腰痛及びびまん性筋骨格痛があった。その後数ヵ月にわたって，疼痛が徐々に増強し，被験者はリウマチ科医のアドバイスで詳細な診断及び理学療法を受けるために入院した。被験者は慢性疼痛症候群と診断され，デュロキセチンの投与が開始された。治験責任医師によると，肥満がリスク因子であった。投与 245 日後，被験者は退院した。

投与された薬剤は，デュロキセチンであった。

The patient's past medications include:

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

Causality for RISANKIZUMAB (Blinded)

---

1) Chronic pain (10049475) (Pain (10033371)) [v.22.1] [10049475]

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 CHRONIC PAIN SYNDROME

- Investigator: Obesity

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ELECTROMYOGRAPHY: Normal

[redacted] **20[redacted] MRI LIVER:** Focal nodular hyperplasia in liver

[redacted] **20[redacted] ULTRASOUND ABDOMEN:** Showed isoreflective lesion in liver for which MRI

[redacted] **20[redacted] ULTRASOUND LEFT SHOULDER:** Calcification supraspinatus tendon

[redacted] 20[redacted] X-RAY LEFT SHOULDER: Acromion type 2

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

[redacted] 20[redacted] X-RAY THORAX: 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
腸閉塞	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Placebo SC Q8W	5[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: SPONDYLOARTHROPATHY	20[redacted]
OTHER: RENAL COLIC	20[redacted]
OTHER: LEFT AXIS DEVIATION AND LOW QRS VOLTAGE	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	6 CIGARETTE	15	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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1
M16006 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57	1

PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 144	[redacted]20[redacted] / 144	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 197	[redacted]20[redacted] / 197	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 256	[redacted]20[redacted] / 256	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 312	[redacted]20[redacted] / 312	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 348	[redacted]20[redacted] / 348	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 368	[redacted]20[redacted] / 368	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 423	[redacted]20[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]
LEKOVIT CA	1.5 mg	QD	Y-M: 20[redacted] / 8
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 8
PREDNISONE	60 mg	QD	Y-M: 20[redacted] / 8
PREDNISONE	52.5 mg	QD	Y-M: 20[redacted] / 18
ULTRACET	0.5 OTHER: CAPSULE	TID	Y-M: 20[redacted] / 22
PREDNISONE	45 mg	QD	Y-M: 20[redacted] / 28
PREDNISONE	37.5 mg	QD	Y-M: 20[redacted] / 38
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 48
PREDNISONE	22.5 mg	QD	Y-M: 20[redacted] / 58
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / 68
PREDNISONE	7.5 mg	QD	Y-M: 20[redacted] / 79
PREDNISONE	7.5 mg	OTHER: ALTERNATE DAYS	Y-M: 20[redacted] / 89

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 Description	INTESTINAL OBSTRUCTION
Preferred Term	腸閉塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 334
Age at AE Onset	5[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 333): NPTST439-PROTEIN C-REACTIVE: 32.39 [0 - 5] MG/L; [redacted]20[redacted] (Rx Day 334): NPTST439-PROTEIN C-REACTIVE: 93.92 [0 - 5] MG/L; [redacted]20[redacted] (Rx Day 335): NPTST439-PROTEIN C-REACTIVE: 189.25 [0 - 5] MG/L; [redacted]20[redacted] (Rx Day 337): NPTST439-PROTEIN C-REACTIVE: 30.02 [0 - 5] MG/L

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 334): ABDOMINAL CT SCAN:DIFFUSE DISTENTION OF SMALL BOWEL LOOPS WITH A CHANGE IN CALIBER IN TRANSITION WITH DISTAL ILEAL FIBROSTENOSANT SEGMENT OF ABOUT 30 CM COMPATIBLE WITH INTESTINAL OBSTRUCTION. FINDINGS CONSISTENT WITH; [redacted]20[redacted] (Rx Day 339): MAGNETIC RESONANCE:THE HYPOINTENSE CIRCUMFERENTIAL THICKENING (ABOUT 30 CM OF THE TERMINAL ILEUM) PERSISTS WITH MARKED LUMINAL STENOSIS WITHOUT PERISTALSIS IN THE CINERM SEQUENCE AND WITHOUT A PATTERN OF ENHANCEMENT OR

AE Stopped Rx Day	368
Duration of AE	35 DAYS
Severity	MILD
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	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，腸閉塞の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，腎仙痛，元喫煙者（1 日 6 本を 15 年間）及び現飲酒者（1 日 2 杯未満）であった。

投与 334 日後，被験者は腸閉塞を発現した。投与 368 日後，腸閉塞は消失した。

投与 334 日後，被験者は激しい腹痛，悪心及び嘔吐のため，入院した。CT スキャン検査，MRI 及び臨床検査が行われた。投与 334 日後，prednisone 60 mg/日の静脈内投与及び抗生物質の

投与が開始された。投与 337 日後，腹痛は消失した。手術は実施されなかった。投与 340 日後，prednisone は経口投与に変更され，抗生物質の投与は終了となった。通常食が開始され，経過は良好であった。投与 341 日後，被験者は退院した。

投与された薬剤は，prednisone，メチルプレドニゾロン及びピペラシリン・タゾバクタム合剤であった。

Causality for RISANKIZUMAB (Blinded)

---

1) Intestinal obstruction (10022687) (Intestinal obstruction (10022687)) [v.23.1] [10022687]

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 INTESTINAL OBSTRUCTION

- Investigator: Not applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL CT SCAN:** Diffuse distention of small bowel loops with a change in caliber in transition with distal ileal fibrostenosant segment of about 30 cm compatible with intestinal obstruction. Findings consistent with small bowel obstruction secondary to ileal fibrostenosal disease.

[redacted] **20[redacted] CRP:** 32.39 MG/L (normal 0.0 to 5.00)

[redacted] **20[redacted] CRP:** 93.92 MG/L (normal 0.0 to 5.00)

[redacted] **20[redacted] CRP:** 189.25 MG/L (normal 0.0 to 5.00)

[redacted] **20[redacted] CRP:** 30.02 MG/L (normal 0.0 to 5.00)

[redacted] **20[redacted] MRI:** The hypointense circumferential thickening (about 30 cm of terminal ileum) persists with marked luminal stenosis without peristalsis in the cineRM sequence and without a pattern of enhancement or diffusion behavior that suggest inflammatory activity. Two other short 2 and 5 cm stenotic segments are identified in the middle ileum and with decreased peristalsis, but without significant mural thickening or inflammatory signs.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
上室性頻脈	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	2[redacted]	MALE	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)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 53	[redacted]20[redacted] / 53	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 143	[redacted]20[redacted] / 143	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 143	[redacted]20[redacted] / 143	1

PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 198	[redacted]20[redacted] / 198	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 198	[redacted]20[redacted] / 198	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 256	[redacted]20[redacted] / 256	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 256	[redacted]20[redacted] / 256	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 316	[redacted]20[redacted] / 316	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 316	[redacted]20[redacted] / 316	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 379	[redacted]20[redacted] / 379	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 379	[redacted]20[redacted] / 379	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 429	[redacted]20[redacted] / 429	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 429	[redacted]20[redacted] / 429	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
MESALAZINE	1500MG mg	TID	Y-M: 20[redacted]-[redacted] / -27
METHYLPREDNISOLONE	40MG mg	QID	Y-M: 20[redacted]-[redacted] / -27

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
NOT REPORTED				

Event #1: Serious Adverse Event

Event Description SUPRAVENTRICULAR TACHYCARDIA
Preferred Term 上室性頻脈
AE Onset Date / Rx Day [redacted]20[redacted] / 140
Age at AE Onset 2[redacted]
Laboratory Testing
[redacted]20[redacted] (Rx Day 140): NPTST153-CPK: 102U/L [38 - 174] U/L; NPTST154-CPK MB: 20 U/L [0 - 24] U/L; NPTST531-TROPONIN: 0,03 [NOT REPORTED - NOT REPORTED] ug/L
Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 140): EKG:SINUS RHYTHM, INDIFFERENT TYPE, IRBBB; EKG HOLTER:SINUS RHYTHM. HEART RATE 47 TO 148/MIN, AVERAGE 72/MIN. SINGLE PALPITATIONS, SHORT EPISODE OF SUPRAVENTRICULAR TACHYCARDIA. NO ST-T CHANGES. NO PATHOLOGICAL PAUSES.

AE Stopped Rx Day	142
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PRECORDIAL PAIN
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

ブルガリア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，上室性頻脈の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，非喫煙者及び非飲酒者であった。

投与 141 日後，被験者は上室性頻脈を発現した。投与 142 日後，上室性頻脈は消失した。

投与 140 日後，被験者は動悸及び胸部圧迫感のため入院した。心電図検査及びホルター心電図検査などの精密検査が行われた。最終診断は上室性頻脈であった。投与 142 日後，症状は消失し，被験者は健康上のリスクなく退院した。

The patient's past medications include:

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

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

Causality for RISANKIZUMAB (Blinded)

---

1) Supraventricular tachycardia (10042604) (Supraventricular tachycardia (10042604)) [v.22.0] [10042604]

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 SUPRAVENTRICULAR TACHYCARDIA

- Investigator: Precordial pain

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] EKG:** sinus rhythm, indifferent position, incomplete rbbb

[redacted] **20[redacted] HOLTER EKG:** Sinus rhythm. Heart rate 47 to 148/min, average 72/min. Single palpitations, short episode of supraventricular tachycardia. No st-t changes. No pathological pauses.

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
回腸狭窄	X			

Treatment Group	Age at M16-006 Study Start	Sex	Race
Placebo SC Q8W	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PSORIASIS	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	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	UNKNOWN	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29	1
M16006 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 62	[redacted]20[redacted] / 62	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 91	[redacted]20[redacted] / 91	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 146	[redacted]20[redacted] / 146	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 202	[redacted]20[redacted] / 202	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 254	[redacted]20[redacted] / 254	1

PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 307 307	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 358 358	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 395 395	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 441 441	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
MESALAZINE	1600 mg	PRN	Y-M: 20[redacted] / -305
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -38

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 Description	ILEAL SUBSTENOSIS
Preferred Term	回腸狭窄
AE Onset Date / Rx Day	[redacted]20[redacted] / 505 (64 DAYS AFTER LAST TREATMENT)
Age at AE Onset	1[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 518): Erythrocytes: 5 [4.3 - 9] 10^12/L; Hemoglobin: 133 [135 - 165] G/L; Leukocytes: 6.2 [3.5 - 9] 10^9/L; Lymphocytes/Leukocytes: 28.5 [11 - 49] %; Neutrophils/Leukocytes: 64 [42 - 85] %

Microbiology

[redacted]20[redacted] (Rx Day 505): OTHER ILUEM(12 CM) AND CECUM HISTOLOGICAL EXAMINATION: Positive-CROHN'S DISEASE IN SEVERE ACTIVITY

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 382): MRI:SUBSTENOSIS OF THE ILEUM AND WALL THICKENING 12 CM UPSTREAM OF THE VALVE; [redacted]20[redacted] (Rx Day 470): COLONOSCOPY:ILEAL SUBSTENOSIS; [redacted]20[redacted] (Rx Day 505): ILEUM RESECTION(15CM) CECUM RESECTION (4 CM) APPENDIX RESECTION (4 CM):SURGICAL RESECTION MARGINS ARE FREE FROM DISEASE

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	WORSENING OF THE STENOSIS
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

イタリア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，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，回腸部分狭窄の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，非喫煙者及び飲酒歴不明であった。

20[redacted]年[redacted]月[redacted]日，非盲検化されたリサンキズマブによるレスキュー治療が開始された。

投与 505 日後，被験者は回腸部分狭窄を発現した。

投与 504 日後，被験者は回腸切除のため，入院した。MRI 及び結腸内視鏡検査が実施された。回腸，盲腸，虫垂切除を行った。投与 509 日後，被験者は良好な状態で退院した。

Causality for RISANKIZUMAB (Blinded)

---

1) Ileal stenosis (10021307) (Ileal stenosis (10021307)) [v.23.1] [10021307]

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) Ileal stenosis (10021307) (Ileal stenosis (10021307)) [v.23.1] [10021307]

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 ILEAL SUBSTENOSIS

- Investigator: Worsening of the stenosis

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

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of ILEAL SUBSTENOSIS

- Investigator: Worsening of the stenosis

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] COLONOSCOPY: ileal substenosis

[redacted] **20[redacted] HEMOGLOBIN:** 13.8 G/DL (normal 13.5 to 16.5)

[redacted] **20[redacted] HISTOLOGICAL EXAMINATION:** Crohn's disease in severe activity

[redacted] **20[redacted] LYMPHOCYTES %:** 28.5 % (normal 11 to 49)

[redacted] **20[redacted] MRI:** Substenosis of the ileum and wall thickening 12 cm upstream of the valve

[redacted] **20[redacted] MRI:** abdominal and pelvic: results not provided

[redacted] **20[redacted] NEUTROPHILS %:** 64 % (normal 42 to 85)

[redacted] **20[redacted] RED BLOOD CELLS:** 5.04 X10**12/L (normal 4.3 to 9)

[redacted] **20[redacted] WBC:** 6.15 X10**3/MCL (normal 3.5 to 9)

[redacted] 20[redacted] WEIGHT: 4[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
腹部膿瘍	X	X		X
胃腸管瘻	X	X		
胃腸の炎症	X	X		

Treatment Group	Age at M16-006 Study Start	Sex	Race
Placebo SC Q8W	3[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: FOLICULITIS	NOT REPORTED
INFLAMMATORY BOWEL DISEASE: PERINEAL FISTULA	20[redacted]
CROHN'S DISEASE	20
INFLAMMATORY BOWEL DISEASE: PERINEAL ABSCESS	20
ANEMIA: ANEMIA AS EIM FOR CD	20
OTHER: ABSCESS OF RIGHT HYPOGASTRIUM ONGOING	20
PEPTIC ULCER DISEASE: MILD BULBITIS - MILD INFLAMMATORY CHANGES IN THE BUBLUS OF DUODENUM	20

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF PERINEAL ABSCESS	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF PERINEAL ABSCESS	20
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	20
CROHN'S DISEASE SURGICAL HISTORY: ADVANCEMENT FLAP	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)
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 31	[redacted]20[redacted] / 31	1
M16006 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 89	[redacted]20[redacted] / 89	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 142	[redacted]20[redacted] / 142	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
INFLIXIMAB	5 mg/kg	Q2M	Y-M: 20[redacted]-
IRON	100 mg	BID	Y-M: 20[redacted]- / 40
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]- / 79
AUGMENTIN	1 g	TID	Y-M: 20[redacted]- / 82
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]- / 82

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
CYLIP	NA OTHER: NA	BID	Y-M: 20[redacted]- / 127	NOT REPORTED
OSELTAMIVIR	75 mg	BID	Y-M: 20[redacted]- / 174	Y-M: 20[redacted]- / 178

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

Event Description INTRA-ABDOMINAL ABSCESS IN THE MIDDLE HYPOGASTRIUM

Preferred Term 腹部膿瘍

AE Onset Date / Rx Day [redacted]20[redacted] / 163 (21 DAYS AFTER LAST TREATMENT)

Age at AE Onset 3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 163): NPTST160-CRP: 136.2 [0 - 10] MG/L

Microbiology

[redacted]20[redacted] (Rx Day 163): STOOL PCR - BASIC VIRAL AND BACTERIA: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 163): ABDOMINAL AND MINOR PELVIS CT SCAN WITH CONTRAST:SEVERE INFLAMATORY CHANGES IN THE RIGHT HYPOGASTRIUM AND A SUSPECTION FOR ABSCESS IN THE PELVIC REGION; [redacted]20[redacted] (Rx Day 176): ABDOMINAL MRI WITH CONTRAST:SMALL

ABSCESS PARARECTALLY RIGHT, INFLAMATORY INFILTRATION WITH MULTIPLE ASCESS COLLECTIONS AND FISTULAS IN THE RIGHT HYPOGASTRIUM, INFLAMATORY CHNAGES OF COLON SIGMOIDEUM; [redacted]20[redacted] (Rx Day 182): ABDOMINAL AND MINOR PELVIS CT SCAN WITH CONTRAST:NO PROGRESSION OF THE ABSCESS IN THE SMALL PELVIS, INFLAMATIORY, SEEVERE INFLAMATORY CHENAGES OF THE RIGHT COLON AND ILEUM

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NONE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

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

Event Description	INFLAMATION CHANGES OF THE BOWEL IN THE RIGHT HYPOGASTRIUM, SEVERAL FISTULAS IN THE RIGHT HYPOGASTRIUM, SEVERAL ABSCESS COLLECTION IN THE RIGHT HYPOGASTRIUM
Preferred Term	腹部膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 176 (34 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 184): NPTST160-CRP: 220 [NOT REPORTED - NOT REPORTED] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 176): MR ENETROCLYSIS:MULTIPLE ABCESS COLLETCTION AND SUSPECTION FOR FISTULAS IN THE LOWER RIGHT HYPOGASTRIUM INT HE AREA OF HEAVY INFLAMATORY CHANGES; [redacted]20[redacted] (Rx Day 185): ABDOMINAL CT WITH CONTRAST:SEVERE INFLAMATORY CHANGES OF SMALL AND LARGE BOWEL IN THE RIGHT HYPOGASTRIUM; AXIAL ILEOSTOMY:AXIAL ILEOSTOMY

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NONE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

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

Event Description	INFLAMATION CHANGES OF THE BOWEL IN THE RIGHT HYPOGASTRIUM, SEVERAL FISTULAS IN THE RIGHT HYPOGASTRIUM, SEVERAL ABSCESS COLLECTION IN THE RIGHT HYPOGASTRIUM