REPORTED] UNIT NOT REPORTED; NPTST291-HYALINE CASTS: PRESENT [NOT REPORTED - NOT REPORTED] NA

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 134): CT:KIDNEY STONE 4MM RIGHT SIDE; [redacted]20[redacted] (Rx Day 140): KIDNEY STENT:RECOVERED; [redacted]20[redacted] (Rx Day 178): KIDNEY STENT REMOVAL:STENT REMOVED

AE Stopped Rx Day	178
Duration of AE	49 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	MEDICAL HISTORY OF RECURRING KIDNEY STONES
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

ドイツ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，腎結石の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，再発性腎結石症，変形性関節症及び喫煙者（1 日 11 本を 30 年間）であった。

投与 130 日後，被験者は腎結石を発現した。

投与 130 日後入院前の，被験者は右側腎臓痛を発現した。投与 134 日後，腎 CT スキャン検査が行われ，右側腎結石が認められた。投与 139 日後，被験者は右側腎臓痛を再度発現した。

投与 140 日後，被験者は右側腎臓痛のため入院した。右側腎臓ステントが留置された。投与 141 日後，被験者は退院した。

投与 178 日後，被験者は入院した。被験者は腎臓ステント除去を受けた。投与 180 日後，被験者は退院した。投与 178 日後，腎結石は消失した。

投与された薬剤は，イブプロフェン及び Novalgin であった。

The patient's past medications include:

BUDENOFALK for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Kidney stone (10023436) (Nephrolithiasis (10029148)) [v.23.1] [10023436]

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 KIDNEY STONE

- Investigator: Medical history of recurring kidney stones

- AbbVie: Event is more likely related to history of pre-existing recurring nephrolithiasis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] BLOOD URINE: Negative

[redacted] **CT SCAN:** Kidney: kidney stone 4mm right side

[redacted] HYALINE CASTS: Present

[redacted] URINE BACTERIA: Few

[redacted] URINE COLOR: Amber

[redacted] 20[redacted] URINE RED BLOOD CELLS: 72000 No units

[redacted] 20[redacted] URINE WHITE BLOOD CELLS: 3000 No units

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	2[redacted]	MALE	WHITE

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
ANEMIA: ANEMIA	20[redacted]
OTHER: ABDOMINAL MASS LOWER ABDOMEN	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)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 59	[redacted]20[redacted] / 59	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 88	[redacted]20[redacted] / 88	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 143	[redacted]20[redacted] / 143	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 198	[redacted]20[redacted] / 198	1

RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 253 253	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 312 312	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 368 368	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / [redacted]20[redacted] / 424 424	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
INFLIXIMAB	5 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	300 mg	OTHER: WK 0,2,6,EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted] / -259

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	SIGMOIDAL COLON STENOSIS
Preferred Term	大腸狭窄
AE Onset Date / Rx Day	[redacted]20[redacted] / 214
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 219): C Reactive Protein: 370 [5 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 214): SIGMA RESECTION:NO EVIDENCE OF DYSPLASIA, NO EVIDENCE OF MALIGNANCY

AE Stopped Rx Day	224
Duration of AE	11 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	WORSENING OF MORBUS CROHN
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

ドイツ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，S 状結腸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，下腹部の腹部腫瘤及び非喫煙者であった。

投与 214 日後，被験者は S 状結腸狭窄を発現した。投与 224 日後，S 状結腸狭窄は消失した。

投与 214 日後，被験者は，S 状結腸狭窄のため，S 状結腸切除の目的で入院した。異形成及び悪性疾患の徴候は認められなかった。投与 224 日後，被験者は退院した。

投与された薬剤は，セフポドキシム及び Metronidazol であった。

The patient's past medications include:

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

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

Causality for RISANKIZUMAB (Blinded)

---

1) Stenosis colon (10041977) (Large intestinal stenosis (10074061)) [v.22.0] [10041977]

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

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

Dechallenge: No

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of SIGMOIDAL COLON STENOSIS

- Investigator: Worsening of morbus Crohn

- AbbVie: Risk factors include pre-existing Crohn's disease and abdominal mass lower abdomen.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 370 MG/L (normal 5 to 5)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

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

Medical History	Onset Year
CROHN'S DISEASE	19[redacted]
OTHER: DYSKINESIA	20[redacted]
OTHER: FATTY LEVER	20[redacted]
OTHER: GASTRITIS	20[redacted]
OTHER: LYMPHNODE INCREASE	20[redacted]
OTHER: PROSTATA CALCIFICATION	20[redacted]
ANEMIA: IRON DEFFICIENCY	20[redacted]
OTHER: SAPHENOUS VARICOSIS	20[redacted]
OTHER: HEMORRHOIDS	20[redacted]
OTHER: CALF CRAMPS	20[redacted]
OTHER: VITAMIN D3 DEFICIENCY	20[redacted]
OTHER: FIBROME BACK	20[redacted]
OTHER: FISTULA PERIANAL	20[redacted]

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

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 31	[redacted] / 31	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted] / 59	[redacted] / 59	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 81	[redacted] / 81	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 130	[redacted] / 130	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 190	[redacted] / 190	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 253	[redacted] / 253	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 305	[redacted] / 305	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 365	[redacted] / 365	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 416	[redacted] / 416	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
CLONAZEPAM	2 mg	TID	Y-M: 20[redacted]
MAGNESIUM	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -121
IRON	1000 mg	PRN	Y-M: 20[redacted] / -91
BUDESONIDE	3 mg	QD	Y-M: 20[redacted] / -54
COLECALCIFEROL	1000 IU	QD	Y-M: 20[redacted] / -31

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
MELGISORB AG	1 OTHER: PCS	PRN	Y-M: 20[redacted] / 432	NOT REPORTED
METAMIZOLE	40 OTHER: DROPS	PRN	Y-M: 20[redacted] / 433	NOT REPORTED
MEROPENEM	1 g	BID	Y-M: 20[redacted] / 433	Y-M: 20[redacted] / 443
VANCOMYCIN	1 g	QD	Y-M: 20[redacted] / 433	Y-M: 20[redacted] / 443
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 433	Y-M: 20[redacted] / 471

ACICLOVIR	1 OTHER: UNIT	BID	Y-M: 20[redacted] / 438	Y-M: 20[redacted] / 448
ACICLOVIR	200 mg	OTHER: FIVE TIMES A DAY	Y-M: 20[redacted] / 438	Y-M: 20[redacted] / 448

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

Event Description	PERIANAL ABSCESS
Preferred Term	肛門膿瘍
AE Onset Date / Rx Day	[redacted] / 432 (16 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted] (Rx Day 432): C Reactive Protein: 292.7 [0.1 - 5] MG/L; Leukocytes: 22.6 [3.9 - 10.2] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted] (Rx Day 432): CT SCAN:ABSCESS PERIANAL; PROCTOSCOPY:PERIANAL ABSCESS; RECTOSCOPY:PERIANAL ABSCESS; SURGERY: INCISION OF ABSCESS:DRAINAGE OF ABSCESS

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

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

ドイツ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，肛門周囲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，腸切除，狭窄形成，元喫煙者，瘻孔切開，肛門周囲瘻及び非飲酒者であった。

投与 432 日後，被験者は肛門周囲膿瘍を発現した。

投与 432 日後，被験者は肛門周囲腫脹，疼痛，発熱，CRP 上昇，及び白血球増加症のため入院した。腹部 CT スキャン検査の結果，肛門周囲膿瘍が認められた。直腸鏡検査／肛門・直腸鏡検査も行われた（結果の詳細不明）。投与 432 日後，被験者は膿瘍を切開し，排膿する手術を受けた。投与 444 日後，被験者は退院した。

投与された薬剤は，バンコマイシン，Novalgin 及びメロペネムであった。

The patient's past medications include:

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

Causality for RISANKIZUMAB (Blinded)

---

1) Perianal abscess (10034447) (Anal abscess (10048946)) [v.24.0] [10034447]

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 PERIANAL ABSCESS

- Investigator: Underlying disease.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 292.7 MG/L (normal 0.1 to 5)

[redacted] **20[redacted] CT SCAN:** perianal abscess

[redacted] **20[redacted] WBC:** 22.6 X10**3/MCL (normal 3.9 to 10.2)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肛門膿瘍	X			X
痔瘻	X			

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

Medical History	Onset Year
OTHER: CONTRACEPTION	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: MOUTH APHTHOUS ULCERS	20[redacted]
CROHN'S DISEASE	20[redacted]

Prior Procedures	Procedure Year
SURGERY: SEBACEOUS CYST RESECTION	19[redacted]
SURGERY: RIGHT ELBOW SURGERY TO CORRECT DISLOCATION	19[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF PERINEAL ABSCESS	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: DRAINAGE OF PERINEAL ABSCESS	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

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

M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	20[redacted] / 57	20[redacted] / 57	1
M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 85	20[redacted] / 85	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 85	20[redacted] / 85	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 113	20[redacted] / 113	1
M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 141	20[redacted] / 141	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 141	20[redacted] / 141	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 169	20[redacted] / 169	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 239	20[redacted] / 239	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 288	20[redacted] / 288	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 344	20[redacted] / 344	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 400	20[redacted] / 400	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 449	20[redacted] / 449	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	20[redacted] / 511	20[redacted] / 511	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]
MESIGYNA	1 OTHER: INJECTION	PRN	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -253
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 113
MACROGOL	4 L	OTHER: UNIQUE DOSE	Y-M: 20[redacted] / 161
FENTANYL	1 ug/kg	OTHER: UNIQUE DOSE	Y-M: 20[redacted] / 162
PROPOFOL	1 mg/kg	OTHER: UNIQUE DOSE	Y-M: 20[redacted] / 162

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
MESIGYNA	1 OTHER: INJECTION	PRN	Y-M: 20[redacted]	ONGOING
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -253	ONGOING

PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / 268	Y-M: 20[redacted] / 268
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 277	Y-M: 20[redacted] / 371
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 277	Y-M: 20[redacted] / 371
MOMETASONE	1 OTHER: PIECE	QD	Y-M: 20[redacted] / 400	Y-M: 20[redacted] / 406
MACROGOL	4 L	OTHER: UNIQUE DOSE	Y-M: 20[redacted] / 560	Y-M: 20[redacted] / 560
FENTANYL	1 ug/kg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 561	Y-M: 20[redacted] / 561
PROPOFOL	1 mg/kg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 561	Y-M: 20[redacted] / 561

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

Event Description	PERIANAL ABSCESS
Preferred Term	肛門膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 268
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx Day 276): TRANSRECTAL ECOGRAPHY:FISTULA WITH PURULENT SECRETION AND ANAL SECRETION; [redacted]20[redacted] (Rx Day 290): COVID-19 TEST:NEGATIVE	
AE Stopped Rx Day	305
Duration of AE	38 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

Event #2: Serious Adverse Event

Event Description	WORSENING OF FISTULA (LOW TRANSSPHINCTER)
Preferred Term	痔瘻
AE Onset Date / Rx Day	[redacted]20[redacted] / 268
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 276): TRANSRECTAL ECOGRAPHY:FISTULA WITH PURULENT SECRETION AND ANAL SECRETION; [redacted]20[redacted] (Rx Day 290): COVID-19 TEST:NEGATIVE

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

アルゼンチン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，瘻孔（低位括約筋貫通）悪化及び肛門周囲膿瘍の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，会陰膿瘍のドレナージ，瘻孔切開，クローン病，会陰膿瘍のドレナージ，非喫煙者及び非飲酒者であった。

投与 268 日後，被験者は瘻孔（低位括約筋貫通）悪化及び肛門周囲膿瘍を発現した。投与 305 日後，肛門周囲膿瘍は消失した。

Week 8（投与 239 日後）時，排膿を伴わない肛門周囲瘻／痔瘻が 2 ヵ所認められた。

投与 276 日後，被験者は経直腸的超音波検査診断を受け，その結果，化膿を伴う瘻孔及び肛門分泌物が認められた。

投与 295 日後，被験者は，膿瘍ドレナージ及び低位括約筋貫通瘻孔ラインの留置を受けるため，入院した。被験者は発熱，肛門痛及び瘻孔分泌物がある状態で来院した。手術後，被験者は，合併症，発熱，排膿や肛門痛もなく，安定していた。投与 295 日後，被験者は経口抗生剤療

法を継続することとし，退院し，帰宅した。

投与された薬剤は，Ciprofloxacine 及びメトロニダゾールであった。

The patient's past medications include:

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

Causality for RISANKIZUMAB (Blinded)

---

1) Trans-sphincteric fistula (10080221) (Anal fistula (10002156)) [v.23.0] [10080221]

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

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

Dechallenge: Not Applicable

2) Perianal abscess (10034447) (Anal abscess (10048946)) [v.23.0] [10034447]

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 WORSENING OF FISTULA (LOW TRANSSPHUNCTER)

- Investigator: Not Applicable

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

Event of PERIANAL ABSCESS

- Investigator:

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **TRANSRECTAL ECHOGRAPHY:** Fistula with purulence and anal secretions.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at M15-991 Study Start	Sex	Race
Placebo SC Q8W	3[redacted]	FEMALE	NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER

Medical History	Onset Year
OTHER: ABDOMINAL PAIN RELATED TO CROHNS	NOT REPORTED
OTHER: ALLERGY TO STICKING PLASTERS	NOT REPORTED
OTHER: ASTHMA	NOT REPORTED
OTHER: CHOLECYSTECOMY	NOT REPORTED
OTHER: VITAMIN D DEFICIENCY	NOT REPORTED
OTHER: FEBRILE CONVULSIONS	19[redacted]
OTHER: MIGRAINES	19[redacted]
ANEMIA: IRON DEICIENT ANEMIA	19[redacted]
OTHER: ECZEMA	19[redacted]
OTHER: NAUSEA RELATED TO CROHNS	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: EPILEPSY	20[redacted]
OTHER: ERYTHEMA NODOSUM	20[redacted]
OTHER: C-DIFF (TEST POSITIVE)	20[redacted]
EYE DISEASE/DISORDER: ANTERIOR UVEITIS	20[redacted]
OTHER: NON SPECIFIC ARTHRALGIA OF HANDS	20[redacted]
OTHER: APHTOUS ULCERS	20[redacted]
OTHER: INTERMITTENT CONSTIPATIOJN	20[redacted]

Prior Procedures	Procedure Year
SURGERY: HERNIA REPAIR	NOT REPORTED
SURGERY: APPENDICETOMY	19[redacted]
SURGERY: ADENOTONSILLECTOMY	19[redacted]
SURGERY: BILATERAL TRIMMING OF INTERIOR TURBINATES	19[redacted]
SURGERY: CAESAREAN SECTION	20[redacted]
SURGERY: CHOLECYSTECOMY	20[redacted]
SURGERY: HERNIA REPAIR	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	20[redacted] / 1	20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	20[redacted] / 29	20[redacted] / 29	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	20[redacted] / 58	20[redacted] / 58	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 85	20[redacted] / 85	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 146	20[redacted] / 146	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 191	20[redacted] / 191	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	20[redacted] / 204	20[redacted] / 204	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 259	20[redacted] / 259	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 309	20[redacted] / 309	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 364	20[redacted] / 364	1
RISANKIZUMAB	360 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
COLECALCIFEROL	1.25 mg	OTHER: MONTHLY	Y-M: 20[redacted]
CYCLIZINE	50 mg	PRN	Y-M: 20[redacted] / -72
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / -72
BUDESONIDE W/FORMOTEROL FUMARATE	2 OTHER: PUFFS	QD	Y-M: 20[redacted] / -24
MEDROXYPROGESTERONE	150 mg	OTHER: 3 MONTHLY	Y-M: 20[redacted] / -24
TRAMADOL	50-100 mg	PRN	Y-M: 20[redacted] / 3

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
COLOXYL WITH SENNA	1-2 OTHER: TABLETS	PRN	Y-M: 20[redacted] / 86	ONGOING
PARACETAMOL	1000 mg	OTHER: ONE OFF DOSE	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 91
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 92

Event #1: Serious Adverse Event

Event Description	CROHNS FLARE
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 90
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day -3562): Creatinine: 54 [45 - 90] UMOL/L; [redacted]20[redacted] (Rx Day -276): Hemoglobin: 109 [115 - 155] G/L; [redacted]20[redacted] (Rx Day 60): Bilirubin: 4 [2 - 20] UMOL/L; Leukocytes: 10 [4 - 11] 10^9/L; Monocytes: 1 [0.2 - 1] 10^9/L; [redacted]20[redacted] (Rx Day 62): Alkaline Phosphatase: 61 [30 - 150] U/L; Basophils: 0.1 [0 - 0.3] 10^9/L; Bilirubin: 4 [2 - 20] UMOL/L; Neutrophils: 5 [1.9 - 7.5] 10^9/L; Potassium: 3.9 [3.5 - 5.2] MMOL/L; Protein: 75 [64 - 83] G/L; Urate: 1900 [3200 - 7700] UMOL/L; [redacted]20[redacted] (Rx Day 63): Alanine Aminotransferase: 9 [0 - 30] U/L; Albumin: 30 [32 - 48] G/L; Basophils: 0 [0 - 0.3] 10^9/L; Hematocrit: 0 [0 - 0] FRACTION OF 1; Leukocytes: 10.5 [4 - 11] 10^9/L; [redacted]20[redacted] (Rx Day 90): Alanine Aminotransferase: 17 [0 - 30] U/L; Albumin: 35 [32 - 48] G/L; Alkaline Phosphatase: 65 [30 - 150] U/L; Basophils: 0.1 [0 - 0.3] 10^9/L; C Reactive Protein: 78 [0 - 5] MG/L; Creatinine: 62 [45 - 90] UMOL/L; Eosinophils: 0.3 [0 - 0.6] 10^9/L; Ery. Mean Corpuscular Hemoglobin: 26 [27 - 33] PG; Ery. Mean Corpuscular Volume: 81 [80 - 99] FL; Hematocrit: 0 [0 - 0] FRACTION OF 1; Hemoglobin: 127 [115 - 155] G/L; Lymphocytes: 2.1 [1 - 4] 10^9/L; NPTST192-EGFR: 90 [78 - 158] 1ML/MIN/1.73M3; NPTST240-GAMMA-GLUTAMYL TRANSFERASE (GGT: 58 [10 - 35] U/L; NPTST253-GLOBULIN: 49 [25 - 41] G/L; Neutrophils: 6.6 [1.9 - 7.5] 10^9/L; Platelets: 561 [150 - 400] 10^9/L; Potassium: 4.1 [3.5 - 5.2] MMOL/L; Protein: 84 [64 - 83] G/L; Sodium: 141 [135 - 145] MMOL/L; Urate: 3200 [3200 - 7700] UMOL/L; [redacted]20[redacted] (Rx Day 91): Alanine Aminotransferase: 10 [0 - 30] U/L; Albumin: 29 [32 - 48] G/L; Alkaline Phosphatase: 58 [30 - 150] U/L; Basophils: 0 [0 - 0.3] 10^9/L; Bilirubin: 7 [2 - 20] UMOL/L; C Reactive Protein: 0.13 [0 - 0.01] MG/L; Eosinophils: 0.2 [0 - 0.6] 10^9/L; Ery. Mean Corpuscular Hemoglobin: 25 [27 - 33] PG; Ery. Mean Corpuscular Volume: 81 [80 - 99] FL; Hematocrit: 0 [0 - 0] FRACTION OF 1; Leukocytes: 9.3 [4 - 11] 10^9/L; Lymphocytes: 1.8 [1 - 4] 10^9/L; Monocytes: 1.3 [0.2 - 1] 10^9/L; NPTST240-GAMMA-GLUTAMYL TRANSFERASE (GGT: 51 [10 - 35] U/L; NPTST253-GLOBULIN: 43 [25 - 41] G/L; Neutrophils: 6 [1.9 - 7.5] 10^9/L; Platelets: 518 [150 - 400] 10^9/L; Potassium: 3.7 [3.5 - 5.2] MMOL/L; Protein: 72 [64 - 83] G/L; Sodium: 132 [135 - 145] MMOL/L; Urate: 1400 [3200 - 7700] UMOL/L; [redacted]20[redacted] (Rx Day 92): Alanine Aminotransferase: 10 [0 - 30] U/L; Albumin: 30 [32 - 48] G/L; C Reactive Protein: 128 [0 - 5] MG/L; Creatinine: 56 [45 - 90] UMOL/L; Eosinophils: 0.3 [0 - 0.6] 10^9/L; Ery. Mean Corpuscular Hemoglobin: 26 [27 - 33] PG; Ery. Mean Corpuscular Volume: 82 [80 - 99] FL; Hematocrit: 0 [0 - 0] FRACTION OF 1; Hemoglobin: 122 [115 - 155] G/L; Leukocytes: 8.2 [4 - 11] 10^9/L; Lymphocytes: 2 [1 - 4] 10^9/L; Monocytes: 0.9 [0.2 - 1] 10^9/L; NPTST240-GAMMA-GLUTAMYL TRANSFERASE (GGT: 48 [10 - 35] U/L; NPTST259-GOBULIN: 45 [25 - 41] G/L; Platelets: 558 [150 - 400] 10^9/L; Sodium: 135 [135 - 145] MMOL/L; [redacted]20[redacted] (Rx Day 93): Alkaline Phosphatase: 60 [35 - 150] U/L; Bilirubin: 3 [2 - 20] UMOL/L; C Reactive Protein: 64 [0 - 5] MG/L; Creatinine: 52 [45 - 90] UMOL/L; Eosinophils: 0.2 [0 - 0.6] 10^9/L; Ery. Mean Corpuscular Hemoglobin: 25 [27 - 33] PG; Ery. Mean Corpuscular Volume: 81 [80 - 99] FL; Hemoglobin: 119 [115 - 155] G/L; Lymphocytes: 2.2 [1 - 4] 10^9/L; Monocytes: 0.9 [0.2 - 1] 10^9/L;

NPTST240-GAMMA-GLUTAMYL TRANSFERASE (GGT: 46 [10 - 35] U/L; NPTST253-GLOBULIN: 44 [25 - 41] G/L; Neutrophils: 7 [4 - 11] 10^9/L; Platelets: 604 [150 - 400] 10^9/L; Potassium: 4.3 [3.5 - 5.2] MMOL/L; Protein: 74 [64 - 83] G/L; Sodium: 139 [135 - 145] MMOL/L; Urate: 2800 [3200 - 7700] UMOL/L

Microbiology

[redacted]20[redacted] (Rx Day 91): BLOOD BLOOD CULTURE: Negative; STOOL FAECAL PCR: Negative; URINE MICROSCOPY AND CULTURE: Negative; STOOL VIBRIO FAECES CULTURE: Negative; [redacted]20[redacted] (Rx Day 92): BLOOD BLOOD CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 90): XRAY ABDOMEN:NAD; [redacted]20[redacted] (Rx Day 92): XRAY CHEST:MINIMAL ATELECTASIS AT THE LEFT LUNG WITH A SMALL EFFUSION. THE LUNGS AND PLEURAL SPACE ARE CLEAR, HEART NORMAL.

AE Stopped Rx Day	93
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHNS FLARE
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

ニュージーランドの治験責任医師からの報告。本被験者は3[redacted]歳女性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，クローン病のフレアの事象を発現した。

Event 1 の臨床経過：

関連する病歴は，熱性痙攣，片頭痛，湿疹，クローン病に関連している悪心，クローン病，クロストリジウム・ディフィシレ感染（検査結果は陽性），クローン病に関連している腹痛，非喫煙者及び飲酒者（1 日 2 杯未満）であった。

投与 90 日後，被験者はクローン病のフレアを発現した。投与 93 日後，クローン病のフレアは消失した。

投与 90 日後，被験者は 2 日間持続している悪心，嘔吐，腹痛，経口摂取に対する耐容不能，及び少量の血便のため入院した。急速輸液，制吐剤，緩下剤，及び鎮痛療法が開始された。被

験者は画像診断，培養，及び血液検査を受けた。投与 93 日後，被験者は退院した。

投与された薬剤は，メトクロプラミド，paracetamol 及び prednisone であった。

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 CROHNS FLARE

- Investigator: Viral Illness

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

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] BLOOD CULTURE: Negative

[redacted] BLOOD CULTURE: Negative

[redacted] **CREATININE:** 62 umol/L (normal 45 to 90)

[redacted] **EGFR:** >90ML/MIN/YEAR

[redacted] GAMMA-GLUTAMYL TRANSFERASE (GGT/Y-GT): 58 U/L (normal 10 to 35)

[redacted] GAMMA-GLUTAMYL TRANSFERASE (GGT/Y-GT): 46 U/L (normal 10 to 35)

[redacted] **GLOBULIN:** 49 G/L (normal 25 to 41)

[redacted] [redacted] **20[redacted] GLOBULIN:** 44 G/L (normal 25 to 41)

[redacted] [redacted] **20[redacted] HEMATOCRIT:** 0.40 % (normal 0.35 to 0.46)

[redacted] [redacted] **20[redacted] HEMOGLOBIN:** 127 G/L (normal 115 to 155)

[redacted] [redacted] **20[redacted] HEMOGLOBIN:** 109 G/L (normal 115 to 155)

[redacted] [redacted] **20[redacted] HEMOGLOBIN:** 119 G/L (normal 115 to 155)

[redacted] [redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 78 MG/L (normal 0 to 5)

[redacted] [redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 131 MG/L (normal 0 to 5)

[redacted] [redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 128 MG/L (normal 0 to 5)

[redacted] [redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 64 MG/L (normal 0 to 5)

[redacted] [redacted] **20[redacted] MCV:** 81 FL (normal 80 to 99)

[redacted] [redacted] **20[redacted] NEUTROPHILS ABS:** 6.6 X10**9/L (normal 1.9 to 7.5)

[redacted] [redacted] **20[redacted] PLATELET COUNT:** 561 X10**9/L (normal 150 to 400)

[redacted] [redacted] **20[redacted] PLATELET COUNT:** 604 X10**9/L (normal 150 to 400)

[redacted] [redacted] **20[redacted] POTASSIUM:** 4.1 MMOL/L (normal 3.5 to 5.2)

[redacted] [redacted] **20[redacted] SODIUM:** 141 MMOL/L (normal 135 to 145)

[redacted] [redacted] **20[redacted] SODIUM:** 132 MMOL/L (normal 135 to 145)

[redacted] [redacted] **20[redacted] SODIUM:** 139 MMOL/L (normal 135 to 145)

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

[redacted] [redacted] **20[redacted] URIC ACID:** 3.2 MMOL/L (normal 3.2 to 7.7)

[redacted] [redacted] 20[redacted] URINE CULTURE: Negative

[redacted] [redacted] **20[redacted] WHITE BLOOD CELLS:** 10 X10**9/L (normal 4 to 11)

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

[redacted] [redacted] **20[redacted] X-RAY CHEST:** Minimal atelectasis at the left lung with a small effusion. The lungs and pleural space are clear, heart normal.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

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

Medical History	Onset Year
OTHER: PSORIASIS	19[redacted]
HYPERTENSION	20
OTHER: INTERMITTENT ARTHRALGIA AFFECTING ELBOWS, KNEES, AND FINGERS	20
OTHER: INTERMITTENT DYSPEPSIA	20
CROHN'S DISEASE	20
OTHER: PAPULAR SKIN RASH FACE/NECK/TRUNK	20
OTHER: INJECTION SITE ERYTHEMA	20
OTHER: INJECTION SITE SWELLING	20
OTHER: HAEMORRHOIDS	20
DEPRESSION	20
OTHER: ERECTILE DYSFUNCTION	20
OTHER: UROSEPSIS	20
OTHER: COLO-URETHRAL FISTULA	20
GOUT: LEFT GREAT TOE AND LEFT KNEE	20
OTHER: MILD CENTRAL LOWER ABDOMINAL TENDERNESS	20
OTHER: DIARRHOEA	20
OTHER: LEFT KNEE EFFUSION	20

Prior Procedures	Procedure Year
SURGERY: RIGHT INGUINAL HERNIA REPAIR	19[redacted]
SURGERY: OPEN MESH REPAIR OF UMBILICAL HERNIA	20
CROHN'S DISEASE HISTORY: COLONOSCOPY	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	5 CIGARETTE	11	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 34	[redacted]20[redacted] / 34	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 62	[redacted]20[redacted] / 62	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 83	[redacted]20[redacted] / 83	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 133	[redacted]20[redacted] / 133	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]
ADALIMUMAB	160 mg	OTHER: ONCE ONLY	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: ONCE ONLY	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
SILDENAFIL	50 mg	PRN	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
CIPROFLOXACIN	250 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: AT WEEKS 0, 2, 6, AND THEN 8-WEEKLY THEREAFTER	Y-M: 20[redacted]
CITALOPRAM	20 mg	QD	Y-M: 20[redacted]
FOLIC ACID	5 mg	OTHER: WEEKLY	Y-M: 20[redacted]
ALLOPURINOL	300 mg	QD	Y-M: 20[redacted] / 2
CANDESARTAN	16 mg	QD	Y-M: 20[redacted] / 2
METHOTREXATE	25 mg	OTHER: WEEKLY	Y-M: 20[redacted] / 61

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
TRAMADOL	100 mg	BID	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 116
TRAMADOL	100 mg	BID	Y-M: 20[redacted] / 118	Y-M: 20[redacted] / 131
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 130

ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 133
MORPHINE	1 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 131
ONDANSETRON	4 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 133
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 146
TRAMADOL	100 mg	BID	Y-M: 20[redacted] / 145	ONGOING
FENTANYL	75 ug	PRN	Y-M: 20[redacted] / 146	Y-M: 20[redacted] / 146
LIDOCAINE	1 OTHER: SPRAY	OTHER: ONCE ONLY	Y-M: 20[redacted] / 146	Y-M: 20[redacted] / 146
MIDAZOLAM	1 mg	PRN	Y-M: 20[redacted] / 146	Y-M: 20[redacted] / 146

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

Event Description	FLARE OF CROHN'S DISEASE
Preferred Term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 98
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 117): C Reactive Protein: 49 [0 - 5] MG/L; Creatinine: 111 [60 - 105] UMOL/L; Leukocytes: 14.1 [4 - 11] 10^9/L; [redacted]20[redacted] (Rx Day 120): NPTST218-FAECAL CALPROTECTIN: 6200 [0 - 50] MG/KG; [redacted]20[redacted] (Rx Day 128): C Reactive Protein: 72 [0 - 5] MG/L; Creatinine: 89 [60 - 105] UMOL/L; Leukocytes: 3 [0 - 10] /HPF; Leukocytes: 23.1 [4 - 11] 10^9/L; Platelets: 549 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 130): C Reactive Protein: 21 [0 - 5] MG/L; Leukocytes: 18.6 [4 - 11] 10^9/L; Platelets: 639 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 131): C Reactive Protein: 16 [0 - 5] MG/L; Leukocytes: 16.7 [4 - 11] 10^9/L; Platelets: 529 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 132): C Reactive Protein: 14 [0 - 5] MG/L; Leukocytes: 19.5 [4 - 11] 10^9/L; Platelets: 596 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 133): C Reactive Protein: 11 [0 - 5] MG/L; Leukocytes: 22.4 [4 - 11] 10^9/L; Platelets: 630 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 134): C Reactive Protein: 8 [0 - 5] MG/L; Leukocytes: 17.2 [4 - 11] 10^9/L; Platelets: 592 [150 - 400] 10^9/L

Microbiology

[redacted]20[redacted] (Rx Day 117): URINE CULTURE: Negative; [redacted]20[redacted] (Rx Day 120): STOOL CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 125): CT SCAN OF ABDOMEN AND PELVIS WITH CONTRAST:NO EVIDENCE OF AN INTRA-ABDOMINAL COLLECTION OR DEFINITE FISTULA FORMATION; [redacted]20[redacted] (Rx Day 128): X-RAY OF CHEST AND ABDOMEN:NORMAL HEART SIZE AND MEDIASTINAL CONTOUR. NO CONSOLIDATION. PLEURAL SPACES APPEAR CLEAR. NO FEATURES OF HEART FAILURE/FLUID OVERLOAD. BILATERAL BRONCHIAL WALL THICKENING. NO EVIDENCE OF PERFORATION O; [redacted]20[redacted] (Rx Day 131): MRI FISTULA:UNCHANGED APPEARANCES OF FISTULA BETWEEN ANAL CANAL AND MEMBRANOUS URETHRA (WHEN COMPARED TO MR FISTULA [redacted] 20[redacted] AND MR PROSTATE [redacted] 20[redacted]); NO DRAINABLE COLLECTION. NO SUPRALEVATOR EXTENSION.; [redacted]20[redacted] (Rx Day 146): FLEXIBLE SIGMOIDOSCOPY:PERIANAL ULCERS, INFLAMMATION (CONGESTION, ERYTHEMA, ULCERATION) FOUND FROM SIGMOID TO TRANSVERSE COLON, MODERATE IN SEVERITY AND WORSENED COMPARED TO PREVIOUS

EXAMINATIONS; UPPER GI ENDOSCOPY:NORMAL OESOPHAGUS, GASTRITIS, NORMAL DUODENUM

AE Stopped Rx Day	167 (34 DAYS AFTER LAST TREATMENT)
Duration of AE	70 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

ニュージーランド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，クローン病のフレアの事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元紙巻タバコ喫煙者（1 日 5 本を 11 年間），クローン病，尿路性敗血症，結腸尿道瘻，軽度の中央下腹部圧痛，下痢及び現軽度飲酒者（1 日 2 杯未満）であった。

投与 98 日後，被験者はクローン病のフレアを発現した。投与 167 日後，クローン病のフレアは消失した。

投与 98 日後，被験者は頻繁に液状便があり，重度の腹痛が悪化し，日常生活に支障を来たしていた。投与 113 日後，被験者は口腔内潰瘍に気付き，軽度の眼痛を発現していた。被験者は食欲減退及び間欠性悪心も発現した。投与 117 日後，被験者は規定外来院し，CRP 上昇，WBC 上昇，体重減少，及びある程度の急性腎機能障害（非重篤）が認められた。被験者は間欠熱も訴えていた。尿路感染（非重篤）に対応するため，シプロフロキサシンの用量が，増量された。尿路感染（非重篤）は，投与 118 日後からの尿道分泌物及び気尿症を伴う結腸尿道瘻の再開口に続発した可能性が高かった。投与 125 日後，CT スキャン検査が行われ，腹腔内貯留は認められなかった。被験者は，疼痛管理のため経口鎮痛療法を受けており，投与 127 日後の夜，経口コルチコステロイドの単回投与を受けた。投与 128 日後の朝，被験者は耐え難い疼痛を発現し，救急治療室を受診した。同日，被験者は入院し，フレアの症状をコントロールするため methylprednisone の静脈内投与を受けた。また，フレアによる結腸尿道瘻の再開口に続発した尿

路感染に対応するため，抗生剤の静脈内投与及び経口投与も受けた。腹部 X 線検査の結果，穿孔や閉塞の徴候は認められなかった。投与 131 日後，瘻孔を精査し，治療計画を支援するため，MRI 検査が行われた。投与 134 日後，被験者は退院した。本事象により治験薬の投与が中止された。

治験薬の投与が完全に中止され，最終投与は投与 133 日後であった。

投与された薬剤は，メトロニダゾール，オンダンセトロン，モルヒネ，paracetamol，セフロキシム，メチルプレドニゾロン，prednisone，トラマドール及びインフリキシマブであった。

The patient's past medications include:

ADALIMUMAB for CROHN'S DISEASE ([redacted])

INFLIXIMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

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

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of FLARE OF CROHN'S DISEASE

- **Investigator:** Not applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD PRESSURE: 120/83 mmHG

[redacted] **20[redacted] CREATININE (BLOOD):** 111 umol/L (normal 60 to 1055)

[redacted] **20[redacted] CREATININE (BLOOD):** 89 umol/L (normal 60 to 1055)

[redacted] **20[redacted] CT SCAN:** No intra-abdominal collection.

[redacted] 20[redacted] FAECAL CALPROTECTIN (STOOL): 6200 UG/G (normal 0 to 5)

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** Perianal ulcers, inflammation (congestion, erythema, ulceration) found from sigmoid to transverse colon, moderate in severity and worsened compared to previous examinations.

[redacted] 20[redacted] HEART RATE: 70 BPM

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 14 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 11 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 8 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN (BLOOD): 49 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN (BLOOD): 72 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN (BLOOD): 21 MG/L (normal 0 to 5)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN (BLOOD): 16 MG/L (normal 0 to 5)

[redacted] **20[redacted] MRI:** Fistula: Unchanged appearances of fistula between anal canal and membranous urethra (when compared to MR fistula [redacted] 20[redacted] and MR prostate [redacted] 20[redacted]); No drainable collection. NO supralevator extension.

[redacted] **20[redacted] PLATELET COUNT (BLOOD):** 549 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT (BLOOD):** 639 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT (BLOOD):** 529 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT (BLOOD):** 596 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT (BLOOD):** 630 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT (BLOOD):** 592 X10**9/L (normal 150 to 400)

[redacted] 20[redacted] STOOL CULTURE: Negative

[redacted] **20[redacted] UPPER GI ENDOSCOPY:** Normal oesophagus, gastritis, normal duodenum.

[redacted] 20[redacted] URINE CULTURE: Negative

[redacted] **20[redacted] WHITE BLOOD CELLS (BLOOD):** 14.1 X10**9/L (normal 4.0 to 11.0)

[redacted] **20[redacted] WHITE BLOOD CELLS (BLOOD):** 23.1 X10**9/L (normal 4.0 to 11.0)

[redacted] **20[redacted] WHITE BLOOD CELLS (BLOOD):** 18.6 X10**9/L (normal 4.0 to 11.0)

[redacted] **20[redacted] WHITE BLOOD CELLS (BLOOD):** 16.7 X10**9/L (normal 4.0 to 11.0)

[redacted] **20[redacted] WHITE BLOOD CELLS (BLOOD):** 19.5 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] WHITE BLOOD CELLS (BLOOD): 22.4 X10**9/L (normal4.0 to 11.0)

[redacted] **20[redacted] WHITE BLOOD CELLS (BLOOD):** 17.2 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] WHITE BLOOD CELLS (URINE): 3 10^6/L (normal 0 to 10)

[redacted] **20[redacted] X-RAY OF CHEST AND ABDOMEN:** Normal heart size and mediastinal contour. No consolidation. Pleural spaces appear clear. NO features of heart failure/fluid overload. Bilateral bronchial wall thickening. No evidence of perforation or obstruction.

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
赤痢菌性胃腸炎	X			X

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

Medical History	Onset Year
OTHER: HETEROZYGOUS HAEMOGLOBIN S	19[redacted]
CROHN'S DISEASE	20
OTHER: RECURRENT PERIANAL FISTULAE	20
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	20
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	20
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	20
OTHER: FALTERING GROWTH	20
ANEMIA: IRON DEFICIENCY ANAEMIA	20
OTHER: PSORIASIS	20
OTHER: CHICKEN POX	20
OTHER: DECREASED BONE DENSITY IN SPINE	20
OTHER: INTERMITTENT ANKLE ARTHRALGIA	20
OTHER: UPPER RESPIRATORY TRACT INFECTION	20
OTHER: INGROWN HAIR RIGHT LOWER BACK/RIGHT UPPER BUTTOCK AREA	20

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: DIAGNOSTIC LAPAROSCOPY FOR CROHN'S DISEASE	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 22	[redacted]20[redacted] / 22	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 22	[redacted]20[redacted] / 22	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64	1
M15991 /RISANKIZUMAB	600 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 155	[redacted]20[redacted] / 155	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 204	[redacted]20[redacted] / 204	1
RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 8 Weeks	[redacted]20[redacted] / 235	[redacted]20[redacted] / 235	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 260	[redacted]20[redacted] / 260	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 316	[redacted]20[redacted] / 316	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 372	[redacted]20[redacted] / 372	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 423	[redacted]20[redacted] / 423	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
AZATHIOPRINE	125 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: AT 0, 2, AND 6 WEEKS, THEN 8 WEEKLY	Y-M: 20[redacted]
INFLIXIMAB	10 mg/kg	Q2M	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	Q2M	Y-M: 20[redacted]
ADALIMUMAB	160 mg	OTHER: ONCE ONLY	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: ONCE ONLY	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]

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
NATAMYCIN	1 %	PRN	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 234
ONDANSETRON	8 mg	OTHER: ONCE	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 225
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 237
TRANSIPEG	4 OTHER: SACHETS	OTHER: ONCE ONLY	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 234
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 236
FENTANYL	100 ug	OTHER: ONCE ONLY	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 235
LIDOCAINE	1 OTHER: APPLICATION	OTHER: ONCE ONLY	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 235
MIDAZOLAM	3 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 235
MIDAZOLAM	5 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 235
DICLOFENAC	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 267
CARBOHYDRATES NOS W/FATS NOS/MINERA	250 mL	PRN	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 491

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

Event Description	SHIGA-TOXIN GASTROENTERITIS
Preferred Term	赤痢菌性胃腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 235

Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 225): C Reactive Protein: 94 [0 - 5] MG/L; [redacted]20[redacted] (Rx Day 234): C Reactive Protein: 53 [0 - 5] MG/L; Hemoglobin: 102 [130 - 175] G/L; NPTST224-FERRITIN: 229 [15 - 170] UG/L; NPTST225-FIBRINOGEN: 5.6 [1.5 - 4] G/L; NPTST310-IRON: 4 [10 - 30] UMOL/L; Platelets: 734 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 235): C Reactive Protein: 39 [0 - 5] MG/L; Hemoglobin: 98 [130 - 175] G/L; NPTST500-SOLUBLE TRANSFERRIN RECEPTOR: 4.4 [2.2 - 5] MG/L; Platelets: 645 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 236): C Reactive Protein: 43 [0 - 5] MG/L; Hemoglobin: 105 [130 - 175] G/L; Platelets: 733 [150 - 400] 10^9/L; [redacted]20[redacted] (Rx Day 248): C Reactive Protein: 22 [0 - 5] MG/L; Hemoglobin: 98 [75 - 130] G/L; NPTST224-FERRITIN: 122 [15 - 170] UG/L; NPTST225-FIBRINOGEN: 5.3 [1.5 - 4] G/L; Platelets: 657 [150 - 400] 10^9/L

Microbiology

[redacted]20[redacted] (Rx Day 226): BLOOD BLOOD CULTURE: Negative; [redacted]20[redacted] (Rx Day 234): BLOOD BLOOD CULTURE: Negative; BLOOD CYTOMEGALOVIRUS: Negative; BLOOD EPSTEINI-BARR VIRUS: Negative; [redacted]20[redacted] (Rx Day 235): STOOL BACTERIA BATHOGENS: Positive-SHIGA TOXIN POSITIVE E.COLI; OTHER GASTRIC BIOPSY CAMPYLOBACTER-LIKE ORGANISM TES: Negative; STOOL CLOSTRIDUM DIFFICILE: Negative; STOOL CRYPTOSPRODIUM: Negative; URINE CULTURE: Negative; OTHER ASCENDING COLON BIOPSY CYTOMEGALOVIRUS: Negative; OTHER SIGMOID COLON BIOPSY CYTOMEGALOVIRUS: Negative; STOOL ENTAMOEBA HISTOLYTICA: Negative; STOOL GIARDIA: Negative; OTHER TERMINAL ILEUM BIOPSY MYCOBACTERIUM TUBERCULOSIS: Negative; STOOL NOROVIRUS: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 227): CT CHEST/ABDO/PELVIS:INCREASED EXTENT OF COLITIS WHEN COMPARED WITH MRI FROM [redacted] [redacted] 20[redacted]. NO EVIDENCE OF MALIGNANCY; [redacted]20[redacted] (Rx Day 234): CHEST/ABDO X-RAY:LUNGS ARE CLEAR BILATERALLY. NO HILAR, MEDIASTINAL OR PLEURAL ABNORMALITY IS SEEN. DILATED LOOPS OF SMALL BOWEL ARE SEEN WITHIN THE LEFT UPPER ABDOMEN, THE APPEARANCES BEING NONSPECIFIC. ELSEWH; [redacted]20[redacted] (Rx Day 235): COLONOSCOPY:MODERATE TO SEVERE PATCHY CROHN'S WITH SEVERE ILEOCAECAL VALVE STENOSIS (MAY BE FIBROSTENOTIC). SES-CD = 22; MUCOSAL INFLAMMATORY CHANGES SECONDARY TO CROHN'S DISEASE. HAS WORSENED SINCE LAST COLONOSC; GASTROSCOPY:SMALL HIATAL HERNIA. LA GRADE A OESOPHAGITIS. ERYTHEMATOUS MUCOSE IN THE CARDIA, PROBABLY SECONDARY TO REFLUX AND HIATUS HERNIA. NORMAL EXAMINED DUODENUM.

AE Stopped Rx Day	242
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

ニュージーランド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，志賀毒素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，αサラセミア形質疑いを伴うヘテロ接合ヘモグロビンS，クローン病，再発性肛門周囲瘻，クロストリジウム・ディフィシレ感染，クロストリジウム・ディフィシレ感染，乾癬，意図しない体重減少，非喫煙者及び禁酒であった。

20[redacted]年[redacted]月[redacted]日から20[redacted]年[redacted]月[redacted]日まで，被験者は盲検化された治験薬の投与を受けた。20[redacted]年[redacted]月[redacted]日，被験者はレスキュー治療のため規定外来院した。20[redacted]年[redacted]月[redacted]日，レスキュー治療としてリサンキズマブの非盲検投与が開始された。

投与235日後，被験者は志賀毒素胃腸炎を発現した。投与242日後，志賀毒素胃腸炎は消失した。

治験責任医師は，被験者は投与の約3年前以降15 kgの意図しない体重減少に気付き，甲状腺機能亢進症や悪性疾患のような体重減少の原因は特定されなかったと報告した。

投与225日後，被験者は，近年意図しない体重減少，排便回数増加及び腹痛，時折嘔吐及び間欠熱が発現していた。被験者の診断検査の結果，炎症マーカー上昇が認められた。投与227日後，被験者はCTスキャン検査を受け，その結果，大腸炎悪化が認められた。

投与234日後，被験者は，精査及び治療のため，あらかじめ計画されていた通り入院した。症状は，最初はクローン病のフレアの徴候と考えられていたが，入院中に，急性症状は志賀毒素感染が原因，又は少なくとも一部は原因となっている可能性が高いことが確定した。身体的診察の結果，クローン病の腸管徴候以外は認められなかった。検査の結果，胸部は問題なし，皮膚，爪，及び口は正常，二重心音を伴う一定の心拍リズム，心雑音なし，軽度の左側圧痛を伴う正常な腹部，並びに脊椎圧痛なし，であった。

治験責任医師によると，被験者に起こりうる免疫抑制が本事象に関連するリスク因子であると判断された。

投与された薬剤は，Fortisipであった。

The patient's past medications include:

ADALIMUMAB for CROHN'S DISEASE ([redacted])

INFLIXIMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Shigella gastroenteritis (10040549) (Gastroenteritis shigella (10017915)) [v.23.1] [10040549]

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

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

Dechallenge: Not Applicable

Causality for RISANKIZUMAB (Open Label)

---

1) Shigella gastroenteritis (10040549) (Gastroenteritis shigella (10017915)) [v.23.1] [10040549]

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 SHIGA-TOXIN GASTROENTERITIS

- **Investigator:** DISEASE PROGRESSION

- **AbbVie:** Event more likely related to ingestion of contaminated food product.

Alternative Etiology for RISANKIZUMAB (Open Label)

Event of SHIGA-TOXIN GASTROENTERITIS

- Investigator: DISEASE PROGRESSION

- AbbVie: Event more likely related to ingestion of contaminated food product.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL X-RAY:** DILATED LOOPS OF SMALL BOWEL ARE SEEN WITHIN THE LEFT UPPER ABDOMEN, THE APPEARANCES BEING NONSPECIFIC. ELSEWHERE THE BOWEL GAS PATTERN IS UNREMARKABLE. NO EVIDENCE OF FREE INTRAPERITONEAL AIR IDENTIFIED

[redacted] ASCENDING COLON BIOPSY: Cytomegalovirus Negative

[redacted] BLOOD CULTURE: Negative

[redacted] BLOOD CULTURE: Negative

[redacted] **CHEST XRAY:** LUNGS ARE CLEAR BILATERALLY. NO HILAR, MEDIASTINAL OR PLEURAL ABNORMALITY IS SEEN.

[redacted] CMV: Negative

[redacted] **COLONOSCOPY:** MODERATE TO SEVERE PATCHY CROHN'S WITH SEVERE ILEOCAECAL VALVE STENOSIS (MAY BE FIBROSTENOTIC). SES-CD = 22; MUCOSAL INFLAMMATORY CHANGES SECONDARY TO CROHN'S DISEASE. HAS WORSENED SINCE LAST COLONOSCOPY IN [redacted].

[redacted] **CT SCAN:** Chest/Abdo/Pelvis: INCREASED EXTENT OF COLITIS WHEN COMPARED WITH MRI FROM [redacted]. NO EVIDENCE OF MALIGNANCY

[redacted] EPSTEIN-BARR VIRUS: Negative

[redacted] **FERRITIN:** 229 MCG/L (normal 15 to 170)

[redacted] **FIBRINOGEN:** 5.6 MCG/L (normal 1.5 to 4.0)

[redacted] **GASTRIC BIOPSY:** CAMPYLOBACTER-LIKE ORGANISM TEST: Negative

[redacted] **GASTROSCOPY:** SMALL HIATAL HERNIA. LA GRADE A OESOPHAGITIS. ERYTHEMATOUS MUCOSE IN THE CARDIA, PROBABLY SECONDARY TO REFLUX AND HIATUS HERNIA. NORMAL EXAMINED DUODENUM.

[redacted] **HEMOGLOBIN:** 105 G/L (normal 130 to 175)

[redacted] **20[redacted] HGB:** 102 G/L (normal 130 to 175)

[redacted] **20[redacted] HGB:** 98 G/L (normal 130 to 175)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 43 MG/L (normal 0 to 5)

[redacted] **20[redacted] HSCRP:** 94 MG/L (normal 0 to 5)

[redacted] **20[redacted] HSCRP:** 53 MG/L (normal 0 to 5)

[redacted] **20[redacted] HSCRP:** 39 MG/L (normal 0 to 5)

[redacted] **20[redacted] HSCRP:** 22 MG/L (normal 0 to 5)

[redacted] **20[redacted] IRON:** 4.0 MCMOL/L (normal 10 to 30)

[redacted] **20[redacted] PLATELET COUNT:** 734 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT:** 645 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT:** 733 X10**9/L (normal 150 to 400)

[redacted] 20[redacted] SIGMOID COLON BIOPSY: Cytomegalovirus Negative

[redacted] 20[redacted] SOLUBLE TRANSFERRIN RECEPTOR: 4.4 MG/L (normal 2.2 to 5.0)

[redacted] **20[redacted] STOOL BACTERIA PATHOGENS:** positive for SHIGA TOXIN POSITIVE E.COLI

[redacted] **20[redacted] STOOL CULTURE:** Negative: NOROVIRUS; Negative: CRYPTOSPORIDIUM; Negative: GIRADIA; Negative: ENTAMOEBA HISTOLYTICA; Negative: CLOSTRIDUM DIFFICILE

[redacted] **20[redacted] TERMINAL ILEUM BIOPSY:** Negative Mycobacterium tuberculosis

[redacted] 20[redacted] URINE CULTURE: Negative

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 360 mg SC Q8W	2[redacted]	MALE	ASIAN

Medical History	Onset Year
GASTROINTESTINAL BLEED: ANAL FISSURES	20[redacted]
CROHN'S DISEASE	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
ANEMIA: IRON DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	20[redacted]
SURGERY: ANAL FISTULA	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	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)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 32	[redacted]20[redacted] / 32	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60	1

RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 88	20[redacted] / 88	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 143	20[redacted] / 143	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 200	20[redacted] / 200	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 253	20[redacted] / 253	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 316	20[redacted] / 316	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 368	20[redacted] / 368	1
RISANKIZUMAB	360 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 421	20[redacted] / 421	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
INFLIXIMAB	5 mg/kg	OTHER: 0.2.6WEEK	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	Q2M	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted] / -123

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
INFLUENZA VACCINE	0.5 mL	QD	Y-M: 20[redacted] / 253	Y-M: 20[redacted] / 253
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 281	Y-M: 20[redacted] / 282
FENTANYL	50 OTHER: MCG	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
GLYCOPYRRONIUM	0.2 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
GRANISETRON	2 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
KETOROLAC	60 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
LABETALOL	20 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
NICARDIPINE	10 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
OXYCODONE	100 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
OXYCODONE	5 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282

PYRIDOSTIGMINE	10 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
RAMOSETRON	0.3 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
RINGOLACT D	1 L	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
RINGOLACT D	500 mL	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
ROCURONIUM	50 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
THIOPENTAL	0.25 g	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 282
MAGNESIUM OXIDE	500 mg	TID	Y-M: 20[redacted] / 283	Y-M: 20[redacted] / 283
LAFUTIDINE	20 mg	BID	Y-M: 20[redacted] / 283	Y-M: 20[redacted] / 289
LOXOPROFEN	180 mg	TID	Y-M: 20[redacted] / 283	Y-M: 20[redacted] / 289

Event #1: Serious Adverse Event

Event Description	ANAL FISTULA
Preferred Term	痔瘻
AE Onset Date / Rx Day	[redacted]20[redacted] / 276
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 281): Albumin: 36 [42 - 50] G/L; C Reactive Protein: 84.2 [1 - 8] MG/L; Hemoglobin: 121 [130 - 170] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 281): PELVIS MRI/CE:1.THREE INTERSPHINCTERIC ANAL FISTULAS AT 1,6,9 O`CLOCK DIRECTION WITH COMMUNICATION 2.TRANS-SPHINCTERIC SINUS TRACT FORMATION AT LEFT SIDE.; [redacted]20[redacted] (Rx Day 282): FISTULECTOMY.:6 SETONS WERE INSERTED.

AE Stopped Rx Day	284
Duration of AE	9 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CD
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

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

Event 1 の臨床経過：

関連する病歴は，痔瘻，瘻孔切開術，胃腸出血（裂肛），クローン病，非喫煙者及び現飲酒者（2杯未満）であった。

投与276日後，被験者は痔瘻を発現した。投与284日後，痔瘻は消失した。

本事象発現前の投与32日後，被験者は痔瘻（非重篤）を発現していた。

投与281日後，被験者は痔瘻再燃のため入院した。疼痛悪化及び肛門からの分泌物が2週間持続していた。被験者は瘻孔切除術のため入院し，6シートンが留置された。投与284日後，被験者は退院した。

投与された薬剤は，メトロニダゾール，シプロフロキサシン及びロキソプロフェンであった。

The patient's past medications include:

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

Causality for RISANKIZUMAB (Blinded)

---

1) Anal fistula (10002156) (Anal fistula (10002156)) [v.22.1] [10002156]

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 FISTULA

- Investigator: CD

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 3.6 G/DL (normal 4.2 to 5)

[redacted] **20[redacted] HEMOGLOBIN:** 12.1 G/DL (normal 13 to 17)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 8.42 mg/dL (normal 0.1 to 0.8)

[redacted] **20[redacted] PEVIC MRI/CE:** 1.THREE INTERSPHINCTERIC ANAL FISTULAS AT 1,6,9 O'CLOCK DIRECTION WITH COMMUNICATION 2.TRANS-SPHINCTERIC SINUS TRACT FORMATION AT LEFT SIDE.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

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

Medical History	Onset Year
CROHN'S DISEASE	20[redacted]
OTHER: HEMOGLOBIN SLIGHTLY BELOW NORMAL RANGE	20[redacted]
OTHER: PERIANAL PAIN	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	3 CIGARETTE	2	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 22	[redacted]20[redacted] / 22	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 50	[redacted]20[redacted] / 50	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20[redacted] / 79	[redacted]20[redacted] / 79	1
M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 79	[redacted]20[redacted] / 79	1
M15991 /RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20[redacted] / 79	[redacted]20[redacted] / 79	1

M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20 / [redacted]20 / 106 106		1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted]20 / [redacted]20 / 134 134		1
M15991 /PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 134 134		1
M15991 /RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 134 134		1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 163 163		1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 163 163		1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 216 216		1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 216 216		1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 274 274		1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 274 274		1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 330 330		1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 330 330		1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 386 386		1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 386 386		1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 442 442		1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 442 442		1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 498 498		1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	[redacted]20 / [redacted]20 / 498 498		1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]-
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]-
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]-
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]-
INFLIXIMAB	5.83 mg/kg	OTHER: 0 WEEK	Y-M: 20[redacted]-
INFLIXIMAB	5.65 mg/kg	OTHER: 2 WEEK	Y-M: 20[redacted]-
INFLIXIMAB	5 mg/kg	Q2M	Y-M: 20[redacted]-

MESALAZINE	1 g	BID	Y-M: 20[redacted]
ARONAMIN C PLUS	1 OTHER: TABLET	BID	Y-M: 20[redacted]
FEROBA	256 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	5.71 mg/kg	Q2M	Y-M: 20[redacted] / -358
VEDOLIZUMAB	300 mg	OTHER: 0,2,6 WEEKS	Y-M: 20[redacted] / -260
VEDOLIZUMAB	300 mg	Q2M	Y-M: 20[redacted] / -162
SUPREP BOWEL PREP	177 mL	QD	Y-M: 20[redacted] / 162

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
ARONAMIN C PLUS	1 OTHER: TABLET	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 257
VITAMINS NOS	1 OTHER: VIAL	QD	Y-M: 20[redacted] / 227	Y-M: 20[redacted] / 231
ALANINE W/ARGININE/ASPARTIC ACID/CA	1 L	QD	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 231
ACETYLCYSTEINE	300 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
EPHEDRINE	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
EPHEDRINE	4 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
FENTANYL	0.2 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
FENTANYL	1 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
NEFOPAM	100 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
PALONOSETRON	0.075 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
PETHIDINE	25 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
PROPOFOL	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
PROPOFOL	100 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
RAMOSETRON	0.3 mg	OTHER: ONCE	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
REMIFENTANIL	1 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
ROCURONIUM	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
ROCURONIUM	100 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231

ROCURONIUM	50 mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 231	Y-M: 20[redacted]-[redacted] / 231
ROCURONIUM	50 mg	QD	Y-M: 20[redacted]-[redacted] / 231	Y-M: 20[redacted]-[redacted] / 231
SUGAMMADEX	200 mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 231	Y-M: 20[redacted]-[redacted] / 231
SUGAMMADEX	200 mg	QD	Y-M: 20[redacted]-[redacted] / 231	Y-M: 20[redacted]-[redacted] / 231
TACHOSIL	2 mL	QD	Y-M: 20[redacted]-[redacted] / 231	Y-M: 20[redacted]-[redacted] / 231
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]-[redacted] / 231	Y-M: 20[redacted]-[redacted] / 232
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted]-[redacted] / 231	Y-M: 20[redacted]-[redacted] / 234
GLUTATHIONE	2400 mg	QD	Y-M: 20[redacted]-[redacted] / 232	Y-M: 20[redacted]-[redacted] / 232
AMINO ACIDS	362 mL	QD	Y-M: 20[redacted]-[redacted] / 232	Y-M: 20[redacted]-[redacted] / 233
ADENOSINE	40 mg	QD	Y-M: 20[redacted]-[redacted] / 232	Y-M: 20[redacted]-[redacted] / 234
CERNEVIT	1 OTHER: VIAL	QD	Y-M: 20[redacted]-[redacted] / 232	Y-M: 20[redacted]-[redacted] / 234
ACETYLCYSTEINE	600 mg	BID	Y-M: 20[redacted]-[redacted] / 232	Y-M: 20[redacted]-[redacted] / 235
SELENIUM	20 mL	QD	Y-M: 20[redacted]-[redacted] / 232	Y-M: 20[redacted]-[redacted] / 235
AMINO ACIDS	724 mL	QD	Y-M: 20[redacted]-[redacted] / 234	Y-M: 20[redacted]-[redacted] / 234

Event #1: Serious Adverse Event

Event Description	PERFORATION OF A-COLON
Preferred Term	大腸穿孔
AE Onset Date / Rx Day	[redacted]20[redacted] / 227
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 227): Albumin: 39 [41 - 51] G/L; Blood Urea Nitrogen: 2.5 [2.9 - 7.1] MMOL/L; C Reactive Protein: 5.83 [0 - 0.6] MG/L; Ery. Mean Corpuscular Hemoglobin: 23.3 [25.6 - 35.5] PG; Ery. Mean Corpuscular Volume: 75.6 [80 - 97.7] FL; Hematocrit: 0.34 [0.34 - 0.5] FRACTION OF 1; Hemoglobin: 103 [140 - 176] G/L; Leukocytes: 3.6 [3.7 - 9.8] 10^9/L; Monocytes/Leukocytes: 14.6 [3.5 - 9.9] %; NPTST334-MCHC: 30.7 [31.6 - 35.8] G/DL; NPTST441-PT(INR): 1.18 [0.9 - 1.14] INR; NPTST442-PT(SEC): 12.5 [9.5 - 12.1] SEC; Platelets: 372 [160 - 362] 10^9/L; [redacted]20[redacted] (Rx Day 230): Ery. Mean Corpuscular Hemoglobin: 23.4 [25.6 - 35.5] PG; Ery. Mean Corpuscular Volume: 76.3 [80 - 97.7] FL; Erythrocytes: 4.3 [4.3 - 5.7] 10^12/L; Hematocrit: 0.33 [0.34 - 0.5] FRACTION OF 1; Hemoglobin: 101 [140 - 176] G/L; Leukocytes: 4.2 [3.7 - 9.8] 10^9/L; Monocytes/Leukocytes: 10.7 [3.5 - 9.9] %; NPTST160-CRP: 1.6 [0 - 0.6] MG/DL; NPTST334-MCHC: 30.7 [31.6 - 35.8] G/DL; Platelets: 394 [160 - 362] 10^9/L; [redacted]20[redacted] (Rx Day 231): Albumin: 40 [41 - 51] G/L; Albumin: 36 [41 - 51] G/L; Blood Urea Nitrogen: 2.6 [2.9 - 7.1] MMOL/L; Creatinine: 61 [62 - 106] UMOL/L; NPTST160-CRP: 1.25 [0 - 0.6] MG/DL; NPTST160-CRP: 0.87 [0 - 0.6] MG/DL; NPTST260-GOT: 57 [16 - 49] IU/L; NPTST524-TOTAL PROTEIN: 6.2 [6.7 - 8.1] G/DL;

[redacted]20[redacted] (Rx Day 232): Albumin: 33 [41 - 51] G/L; Blood Urea Nitrogen: 1.7 [2.9 - 7.1] MMOL/L; Creatinine: 50 [62 - 106] UMOL/L; Ery. Mean Corpuscular Hemoglobin: 23.5 [25.6 - 35.5] PG; Ery. Mean Corpuscular Volume: 77.3 [80 - 97.7] FL; Erythrocytes: 4 [4.3 - 5.7] 10^12/L; Glucose: 7.9 [3.9 - 5.5] MMOL/L; Hematocrit: 0.31 [0.34 - 0.5] FRACTION OF 1; Hemoglobin: 94 [140 - 176] G/L; Leukocytes: 9.3 [3.7 - 9.8] 10^9/L; Lymphocytes/Leukocytes: 9.4 [20.3 - 50.8] %; NPTST160-CRP: 1.92 [0 - 0.6] MG/DL; NPTST334-MCHC: 30.4 [34.6 - 35.8] G/DL; NPTST368-N.SEG: 82.3 [38.1 - 71.5] %; NPTST453-RDW: 15.4 [11.7 - 15.2] %; NPTST524-TOTAL PROTEIN: 5.9 [6.7 - 8.1] G/DL; Platelets: 378 [160 - 362] 10^9/L; [redacted]20[redacted] (Rx Day 234): Albumin: 30 [41 - 51] G/L; Blood Urea Nitrogen: 1.3 [2.9 - 7.1] MMOL/L; Creatinine: 44 [62 - 106] UMOL/L; Ery. Mean Corpuscular Hemoglobin: 23.5 [25.6 - 35.5] PG; Ery. Mean Corpuscular Volume: 77.3 [80 - 97.7] FL; Erythrocytes: 3.8 [4.3 - 5.7] 10^12/L; Hematocrit: 0.3 [0.34 - 0.5] FRACTION OF 1; Hemoglobin: 90 [140 - 176] G/L; Leukocytes: 3.5 [3.7 - 9.8] 10^9/L; Lymphocytes/Leukocytes: 19.9 [20.3 - 50.8] %; Monocytes/Leukocytes: 11.4 [3.5 - 9.9] %; NPTST160-CRP: 1.79 [0 - 0.6] MG/DL; NPTST334-MCHC: 30.4 [31.6 - 35.8] G/DL; NPTST453-RDW: 16.1 [11.7 - 15.2] %; NPTST524-TOTAL PROTEIN: 5.3 [6.7 - 8.1] G/DL; [redacted]20[redacted] (Rx Day 236): Albumin: 34 [41 - 51] G/L; Blood Urea Nitrogen: 2 [2.9 - 7.1] MMOL/L; Creatinine: 58 [62 - 106] UMOL/L; Ery. Mean Corpuscular Hemoglobin: 23.4 [25.6 - 35.5] PG; Ery. Mean Corpuscular Volume: 77.8 [80 - 97.7] FL; Erythrocytes: 4.1 [4.3 - 5.7] 10^12/L; Hematocrit: 0.32 [0.34 - 0.5] FRACTION OF 1; Hemoglobin: 96 [140 - 176] G/L; Leukocytes: 3.6 [3.7 - 9.8] 10^9/L; Lymphocytes/Leukocytes: 19.9 [20.3 - 50.8] %; Monocytes/Leukocytes: 13.2 [3.5 - 9.9] %; NPTST334-MCHC: 30.1 [31.6 - 35.8] G/DL; NPTST453-RDW: 16.4 [11.7 - 15.2] %; NPTST524-TOTAL PROTEIN: 5.8 [6.7 - 8.1] G/DL; Platelets: 412 [160 - 362] 10^9/L

Microbiology

[redacted]20[redacted] (Rx Day 227): BLOOD BLOOD CULTURE 1ST: Negative; BLOOD BLOOD CULTURE 2ND: Negative; [redacted]20[redacted] (Rx Day 228): URINE CULTURE & MIC <URINE,VOIDED>: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 225): ABDOMEN & PELVIS MDCT:-PERFORATION OF A-COLON:FORMING IRREGULAR INFLAMMATORY TISSUE IN MESENTERY WITH POSSIBLE ADHESION OF ADJACENT ILEUM -NO CHANGE OF MULTIFOCAL WALL THICKENING AND STRICTURE IN IC VALVE AND ILEUM -NO C; [redacted]20[redacted] (Rx Day 227): ABDOMEN FLAT / UPRIGHT VIEW:NON-SPECIFIC BOWEL GAS PATTERN.; CHEST PA VIEW:NO ACTIVE LUNG LESIONS.; PORTABLE EKG:SINUS RHYTHM. INCOMPLETE RIGHT BUNDLE BRANCH BLOCK. BASELINE WANDER IN LEAD(S) V6; [redacted]20[redacted] (Rx Day 230): EKG:SINUSS RHYTHM. NONSPECIFIC INTRAVENTRICULAR CONDUCTION DELAY. BORDELINE T ABNOMALITIES, ANTERIOR LEAS. BASELINE WANDER IS LEAD(S) V1,V2,V3,V6.; [redacted]20[redacted] (Rx Day 232): ABDOMEN FLAT / UPRIGHT VIEW:POST OP PNEUMOPERITONEUM; ABDOMEN FLAT / UPRIGHT VIEW:POST OP PNEUMOPERITONEUM; BIOPSY(SPECIMEN):ASCENDING COLON, CECUM, APPENDIX, AND TERMINAL ILEUM, RIGHT HEMICOLECTOMY: . CONSISTENT WITH CROHN'S DISEASE OF COLON WITH 1) COLONIC STRICTURE 2) INFLAMMATORY PSEUDOPOLYPS; CHEST PA VIEW:BOTH SUBPHRENIC FREE GAS. NO ACTIVE LUNG LESIONS.; CHEST PA VIEW:BOTH SUBPHRENIC FREE GAS. NO ACTIVE LUNG LESIONS.; [redacted]20[redacted] (Rx Day 233): ABDOMEN FLAT / UPRIGHT VIEW:POST OP PNEUMOPERITONEUM; ABDOMEN FLAT / UPRIGHT VIEW:POST OP PNEUMOPERITONEUM; [redacted]20[redacted] (Rx Day 234): ABDOMEN FLAT / UPRIGHT VIEW:POST OP PNEUMOPERITONEUM; CHEST PA VIEW:BOTH SUBPHRENIC FREE GAS. NO ACTIVE LUNG LESIONS.; [redacted]20[redacted] (Rx Day 236): ABDOMEN FLAT / UPRIGHT VIEW:POST OP PNEUMOPERITONEUM

AE Stopped Rx Day	238
Duration of AE	12 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SHORT-TERM DETERIORATION OF 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

韓国の治験責任医師からの報告。本被験者は3[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，上行結腸穿孔の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，元紙巻タバコ喫煙者（1 日 3 本を 2 年間），基準範囲よりわずかに低値なヘモグロビン，肛門周囲痛及び元アルコール摂取（1 日 2 杯未満）であった。

投与 227 日後，被験者は上行結腸穿孔を発現した。投与 238 日後，上行結腸穿孔は消失した。

治験開始前から，被験者は右上腹部の不快感を発現していた。

不明日，腹痛が悪化した。投与 225 日後，被験者は腹部及び骨盤部 MDCT を受け，その結果，隣接している回腸に起こりうる癒着を伴い，腸間膜内に不規則な炎症組織を形成している上行結腸穿孔が認められた。投与 227 日後，被験者は精査のため入院した。被験者は絶食となり，抗生剤が投与された。投与 232 日後，被験者は右半結腸切除を受けた。投与 238 日後，被験者は退院した。

投与された薬剤は，Triaxone，Trizele，ガスター，Periolimel N4E，Omapone Peri，Spatam，アロキシ，ペチジン塩酸塩，Remiva，フェンタニル，Acupan，Luthione，Selenase T pro，Cernevit，ATP，Tamipool 及び Tridol であった。

The patient's past medications include:

INFLIXIMAB for CROHN'S DISEASE ([redacted])

VEDOLIZUMAB for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Perforation of colon (10034418) (Large intestine perforation (10023804)) [v.23.0] [10034418]

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 PERFORATION OF A-COLON

- Investigator: Short-term deterioration of disease.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMEN & PELVIS MDCT:** Perforation of a colon: forming irregular inflammatory tissue in mesentery with possible adhesion of adjacent ileum.

[redacted] **ABDOMINAL X RAY:** Non-specific bowel gas pattern.

[redacted] **ABDOMINAL X RAY:** Post op pneumoperitoneum.

[redacted] **ABDOMINAL X RAY:** Post op pneumoperitoneum.

[redacted] **ABDOMINAL X RAY:** Post op pneumoperitoneum.

[redacted] **ABDOMINAL X RAY:** Post op pneumoperitoneum.

[redacted] **ALBUMIN:** 3.9 G/DL (normal 4.1 to 5.1)

[redacted] **ALBUMIN:** 3.6 G/DL (normal 4.1 to 5.1)

[redacted] **ALBUMIN:** 4.0 G/DL (normal 4.1 to 5.1)

[redacted] **ALBUMIN:** 3.3 G/DL (normal 4.1 to 5.1)

[redacted] **ALBUMIN:** 3.0 G/DL (normal 4.1 to 5.1)

[redacted] **20**[redacted] **ALBUMIN:** 3.4 G/DL (normal 4.1 to 5.1)

[redacted] **20**[redacted] **BIOPSY:** ASCENDING COLON, CECUM, APPENDIX, AND TERMINAL ILEUM, RIGHT HEMICOLECTOMY: CONSISTENT WITH CROHN'S DISEASE OF COLON WITH 1) COLONIC STRICTURE 2) INFLAMMATORY PSEUDOPOLYPS 3) TRANSMURAL INFLAMMATION WITH LYMPHOID AGGREGATES THROUGHOUT BOWEL WALL 4) FOCAL GRANULOMATOUS LESION 5) APPENDEX: UNREMARKABLE 6) RESECTION MARGINS: NO SIGNIFICANT INFLAMMATORY REACTION 7) REGIONAL LYMPH NODES: UNREMARKABLE (0/8)

[redacted] 20[redacted] BLOOD CULTURE: Negative

[redacted] 20[redacted] BLOOD UREA NITROGEN: 7 mg/dL (normal 8 to 20)

[redacted] 20[redacted] BLOOD UREA NITROGEN: 7.4 mg/dL (normal 8 to 20)

[redacted] 20[redacted] BLOOD UREA NITROGEN: 4.8 mg/dL (normal 8 to 20)

[redacted] 20[redacted] BLOOD UREA NITROGEN: 3.6 mg/dL (normal 8 to 20)

[redacted] 20[redacted] BLOOD UREA NITROGEN: 5.7 mg/dL (normal 8 to 20)

[redacted] **20**[redacted] **C REACTIVE PROTEIN:** 0.87 mg/dL (normal 0 to 0.6)

[redacted] **20**[redacted] **C REACTIVE PROTEIN:** 1.25 mg/dL (normal 0 to 0.6)

[redacted] **20**[redacted] **CHEST PA VIEW:** Both subphrenic free gas. No active lung lesions.

[redacted] **20**[redacted] **CHEST X RAY:** No active lung lesions.

[redacted] **20**[redacted] **CHEST X RAY:** Both subphrenic free gas. No active lung lesions.

[redacted] **20**[redacted] **CREATININE:** 0.69 mg/dL (normal 0.7 to 1.2)

[redacted] **20**[redacted] **CREATININE:** 0.57 mg/dL (normal 0.7 to 1.2)

[redacted] **20**[redacted] **CREATININE:** 0.50 mg/dL (normal 0.7 to 1.2)

[redacted] **20**[redacted] **CREATININE:** 0.66 mg/dL (normal 0.7 to 1.2)

[redacted] **20**[redacted] **CRP:** 1.60 mg/dL (normal 0 to 0.6)

[redacted] **20**[redacted] **EKG:** SINUS RHYTHM. INCOMPLETE RIGHT BUNDLE BRANCH BLOCK. BASELINE WANDER IN LEAD(S) V6

[redacted] **20**[redacted] **EKG:** SINUS RHYTHM. NONSPECIFIC INTRAVENTRICULAR CONDUCTION DELAY. BORDELINE T ABNOMALITIES, ANTERIOR LEAS. BASELINE WANDER IS LEAD(S) V1,V2,V3,V6.

[redacted] **20**[redacted] **GLUCOSE:** 143 mg/dL (normal 70 to 99)

[redacted] **20**[redacted] **GOT:** 57 IU/L (normal 16 to 49)

[redacted] **20[redacted] HEMATOCRIT:** 33.5 % (normal 34.3 to 49.9)

[redacted] **20[redacted] HEMATOCRIT:** 32.9 % (normal 34.3 to 49.9)

[redacted] **20[redacted] HEMATOCRIT:** 30.9 % (normal 34.3 to 49.9)

[redacted] **20[redacted] HEMATOCRIT:** 29.6 % (normal 34.3 to 49.9)

[redacted] **20[redacted] HEMATOCRIT:** 31.9 % (normal 34.3 to 49.9)

[redacted] **20[redacted] HEMOGLOBIN:** 10.3 G/DL (normal 14 to 17.6)

[redacted] **20[redacted] HEMOGLOBIN:** 10.1 G/DL (normal 14.0 to 17.6)

[redacted] **20[redacted] HEMOGLOBIN:** 9.4 G/DL (normal 14.0 to 17.6)

[redacted] **20[redacted] HEMOGLOBIN:** 9.0 G/DL (normal 14.0 to 17.6)

[redacted] **20[redacted] HEMOGLOBIN:** 9.6 G/DL (normal 14.0 to 17.6)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 5.83 MG/L (normal 0 to 0.6)

[redacted] **20[redacted] INR:** 1.18 no unit (normal 0.90 to 1.14)

[redacted] **20[redacted] LYMPHOCYTES:** 9.4 % (normal 20.3 to 50.8)

[redacted] **20[redacted] LYMPHOCYTES:** 19.9 % (normal 20.3 to 50.8)

[redacted] **20[redacted] LYMPHOCYTES:** 19.9 % (normal 20.3 to 50.8)

[redacted] **20[redacted] MCH:** 23.3 PG (normal 25.6 to 35.5)

[redacted] **20[redacted] MCH:** 23.4 PG (normal 25.6 to 35.5)

[redacted] **20[redacted] MCH:** 23.5 PG (normal 25.6 to 35.5)

[redacted] **20[redacted] MCH:** 23.5 PG (normal 25.6 to 35.5)

[redacted] **20[redacted] MCH:** 23.4 PG (normal 25.6 to 35.5)

[redacted] **20[redacted] MCHC:** 30.7 G/DL (normal 31.6 to 35.8)

[redacted] **20[redacted] MCHC:** 30.7 G/DL (normal 31.6 to 35.8)

[redacted] **20[redacted] MCHC:** 30.4 G/DL (normal 31.6 to 35.8)

[redacted] **20[redacted] MCHC:** 30.4 G/DL (normal 31.6 to 35.8)

[redacted] **20[redacted] MCHC:** 30.1 G/DL (normal 31.6 to 35.8)

[redacted] **20[redacted] MCV:** 75.6 FL (normal 80 to 97.7)

[redacted] **20[redacted] MCV:** 76.3 FL (normal 80.0 to 97.7)

[redacted] **20[redacted] MCV:** 77.3 FL (normal 80.0 to 97.7)

[redacted] **20[redacted] MCV:** 77.3 FL (normal 80.0 to 97.7)

[redacted] **20[redacted] MCV:** 77.8 FL (normal 80.0 to 97.7)

[redacted] **20[redacted] MONOCYTES:** 10.7 % (normal 3.5 to 9.9)

[redacted] **20[redacted] MONOCYTES:** 11.4 % (normal 3.5 to 9.9)

[redacted] **20[redacted] MONOCYTES:** 13.2 % (normal 3.5 to 9.9)

[redacted] 20[redacted] LYMPHOCYTE PERCENTAGE: 14.6 % (normal 3.5 to 9.9)

[redacted] **20[redacted] N SEG:** 82.3 % (normal 38.1 to 71.5)

[redacted] **20[redacted] PLATELET COUNT:** 372 X10**3/MM**3 (normal 160 to 362)

[redacted] **20[redacted] PLATELET COUNT:** 394 X10**3/MM**3 (normal 160 to 362)

[redacted] **20[redacted] PLATELET COUNT:** 378 X10**3/MM**3 (normal 160 to 362)

[redacted] **20[redacted] PLATELET COUNT:** 412 X10**3/MM**3 (normal 160 to 362)

[redacted] **20[redacted] PT:** 12.5 SEC (normal 9.5 to 12.1)

[redacted] **20[redacted] RDW:** 15.4 % (normal 11.7 to 15.2)

[redacted] **20[redacted] RDW:** 16.1 % (normal 11.7 to 15.2)

[redacted] **20[redacted] RDW:** 16.4 % (normal 11.7 to 15.2)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.31 X10**6/MCL (normal 4.34 to 5.70)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.0 X10**6/MCL (normal 4.34 to 5.70)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.83 X10**6/MCL (normal 4.34 to 5.70)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.10 X10**6/MCL (normal 4.34 to 5.70)

[redacted] **20[redacted] TOTAL PROTEIN:** 6.2 G/DL (normal 6.7 to 8.1)

[redacted] **20[redacted] TOTAL PROTEIN:** 5.9 G/DL (normal 6.7 to 8.1)

[redacted] **20[redacted] TOTAL PROTEIN:** 5.3 G/DL (normal 6.7 to 8.1)

[redacted] **20[redacted] TOTAL PROTEIN:** 5.8 G/DL (normal 6.7 to 8.1)

[redacted] 20[redacted] URINE CULTURE: Negative

[redacted][redacted] **20**[redacted] **WHITE BLOOD CELLS:** 3.64 X10**3/MM**3 (normal 3.7 to 9.8)

[redacted][redacted] **20**[redacted] **WHITE BLOOD CELLS:** 4.21 X10**3/MM**3 (normal 3.7 to 9.8)

[redacted][redacted] **20**[redacted] **WHITE BLOOD CELLS:** 3.51 X10**3/MM**3 (normal 3.7 to 9.8)

[redacted][redacted] **20**[redacted] **WHITE BLOOD CELLS:** 3.56 X10**3/MM**3 (normal 3.7 to 9.8)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
イレウス	X			
大腸狭窄	X			

Treatment Group	Age at M15-991 Study Start	Sex	Race
Risankizumab 180 mg SC Q8W	2[redacted]	FEMALE	ASIAN

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
DIABETES MELLITUS	20[redacted]
OTHER: GOITER	20[redacted]
OTHER: CHRONIC GASTRITIS	20[redacted]
OTHER: DIARRHEA	20[redacted]
INFLAMMATORY BOWEL DISEASE: INFLAMMATORY BOWEL DISEASE	20[redacted]
OTHER: EXTERNAL HEMORRHOID	20[redacted]
OTHER: ACUTE GASTROENTERITIS	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: CONSTIPATION DUE TO COLON STENOSIS	20[redacted]
OTHER: PRACTISING TRUE ABSTINENCE	20[redacted]
OTHER: URINE INFECTION WITHOUT SPECIFIC SYMPTOMS	20[redacted]

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

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

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

M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 28	20[redacted] / 28	1
M15991 /RISANKIZUMAB	1200 MG	INTRAVENOUS	Every 4 Weeks	20[redacted] / 56	20[redacted] / 56	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 85	20[redacted] / 85	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 85	20[redacted] / 85	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 140	20[redacted] / 140	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 140	20[redacted] / 140	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 196	20[redacted] / 196	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 196	20[redacted] / 196	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 252	20[redacted] / 252	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 252	20[redacted] / 252	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 305	20[redacted] / 305	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 305	20[redacted] / 305	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 361	20[redacted] / 361	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 361	20[redacted] / 361	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 420	20[redacted] / 420	1
RISANKIZUMAB	180 MG	SUBCUTANEOUS	Every 8 Weeks	20[redacted] / 420	20[redacted] / 420	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	160 mg	OTHER: STAT	Y-M: 20[redacted] / -268
ADALIMUMAB	80 mg	OTHER: STAT	Y-M: 20[redacted] / -253
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted] / -239
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -46
IRON	100 mg	QD	Y-M: 20[redacted] / 11
LACTULOSE	20 mL	BID	Y-M: 20[redacted] / 11
LACTULOSE	30 mL	TID	Y-M: 20[redacted] / 56
MAGNESIUM OXIDE	500 mg	TID	Y-M: 20[redacted] / 56

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	100 mg	QD	Y-M: 20[redacted] / 11	NOT REPORTED
LACTULOSE	30 mL	TID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 286
ULTRACET	37.5 mg	QID	Y-M: 20[redacted] / 210	NOT REPORTED
BENAZON	20 g	BID	Y-M: 20[redacted] / 266	NOT REPORTED
LACTULOSE	30 mL	BID	Y-M: 20[redacted] / 375	NOT REPORTED
PARACETAMOL	500 mg	OTHER: Q6HPRN	Y-M: 20[redacted] / 442	Y-M: 20[redacted] / 443
DEXTROMETHORPHAN	15 mg	TID	Y-M: 20[redacted] / 474	Y-M: 20[redacted] / 483
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / 474	Y-M: 20[redacted] / 483

Event #1: Serious Adverse Event

Event Description	COLON SYMPTOMATIC STRICTURING
Preferred Term	大腸狭窄
AE Onset Date / Rx Day	[redacted]20[redacted] / 287
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 287): Activated Partial Thromboplastin Time: 28 [26 - 33] SEC; Albumin: 41 [35 - 57] G/L; Bilirubin: 7 [5 - 17] UMOL/L; Creatinine: 44 [53 - 115] UMOL/L; Ery. Mean Corpuscular Hemoglobin: 17.6 [26 - 34] PG; Ery. Mean Corpuscular Volume: 63.9 [80 - 100] FL; Erythrocytes: 4.4 [3.8 - 5] 10^12/L; Hematocrit: 0.28 [0.36 - 0.45] FRACTION OF 1; Hemoglobin: 77 [108 - 149] G/L; Leukocytes: 3.3 [3.5 - 9.1] 10^9/L; Lymphocytes/Leukocytes: 24.8 [21.3 - 50.2] %; Monocytes/Leukocytes: 5.5 [2.7 - 7.6] %; Platelets: 340 [150 - 361] 10^9/L; Potassium: 3.6 [3.5 - 5.1] MMOL/L; Prothrombin Time: 11 [10 - 12] SEC; Sodium: 138 [136 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 287): COLONOSCOPY AND BALLOON DILATATION:BALLOON DILATATION WITH SUCCESS, NO ACTIVE AND IMMEDIATELY PERFORATION NOTED.

AE Stopped Rx Day	289
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	HOSPITALIZATION DUE TO BALLOON DILATATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	COLON SYMPTOMATIC STRICTURE
Preferred Term	大腸狭窄
AE Onset Date / Rx Day	[redacted]20[redacted] / 440 (20 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 440): Erythrocytes: 5 [3.8 - 5.3] 10^12/L; Hemoglobin: 79 [110 - 152] G/L; Leukocytes: 4.2 [3.3 - 9.2] 10^9/L; Platelets: 460 [150 - 378] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 440): COLONOSCOPY AND BALLOON DILATATION:CROHN'S DISEASE WITH STENOSIS, S/P BALLON DILATATION

AE Stopped Rx Day	443 (23 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	HOSPITALIZATION DUE TO BALLOON DILATATION

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

Event #3: Serious Adverse Event

Event Description	ILEUS
Preferred Term	イレウス
AE Onset Date / Rx Day	[redacted] / 473 (53 DAYS AFTER LAST TREATMENT)
Age at AE Onset	[redacted]

Laboratory Testing

[redacted] (Rx Day 473): Ery. Mean Corpuscular Hemoglobin: 17.9 [25.5 - 33.2] PG; Ery. Mean Corpuscular Volume: 64.5 [80.9 - 99.3] FL; Hematocrit: 0.34 [0.35 - 0.46] FRACTION OF 1; Hemoglobin: 94 [110 - 152] G/L; Leukocytes: 5 [3.3 - 9.2] 10^9/L; Lipase: 9 [11 - 82] U/L; Lymphocytes/Leukocytes: 10.2 [18 - 48.8] %; NPTST334-MCHC: 27.8 [31 - 34.9] G/DL; NPTST454-RDW-CV: 25.4 [11.6 - 15] %; NPTST489-SEGMENT WBC: 82.2 [41.6 - 74.4] %; Sodium: 135 [136 - 145] MMOL/L; [redacted] (Rx Day 474): C Reactive Protein: 22.7 [1 - 3] MG/L; NPTST213-ESR 1HR: 57 [20 - 20] MM/H

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted] (Rx Day 473): KUB ABDOMINAL:ILEUS; [redacted] (Rx Day 474): KUB ABDOMINAL:PROMINENT BOWEL GAS WITH BOWEL DILATATION, SUGGESTIVE OF ILEUS. OBSCURED BILATERAL PSOAS MUSCLES.; [redacted] (Rx Day 475): KUB ABDOMINAL:CLEAR BILATERAL PSOAS SHADOWS. INCREASED BOWEL GAS IN THE ABDOMEN. NO DEFINITE RADIOPAQUE STONES. NO EVIDENCE OF DESTRUCTIVE BONY LESION AT THE SPINE. MILD SUBCHONDRAL SCLEROSIS AT BILATERAL SACROILIA

AE Stopped Rx Day	476 (56 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

台湾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，症候性結腸狭窄の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，糖尿病，鉄欠乏性貧血，慢性胃炎，下痢，炎症性腸疾患，外痔核，急性胃腸炎，クローン病（結腸疾患，狭窄性），結腸狭窄による便秘，非喫煙者及び禁酒であった。

投与 287 日後，被験者は症候性結腸狭窄を発現した。投与 289 日後，症候性結腸狭窄は消失した。

投与 287 日後，被験者は，直腸狭窄及び S 状結腸狭窄による排便困難を訴えて，入院した。同日，被験者は回腸結腸内視鏡検査及び直腸バルーン拡張術を受け，成功した。穿孔は認められず，生検が採取された。被験者は輸血を受けた。投与 289 日後，被験者は退院した。

投与された薬剤は，濃厚赤血球であった。

The patient's past medications include:

ADALIMUMAB for CROHN'S DISEASE ([redacted])

MESALAMINE for CROHN'S DISEASE

Causality for RISANKIZUMAB (Blinded)

---

1) Colonic stricture (10010005) (Large intestinal stenosis (10074061)) [v.24.0] [10010005]

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 COLON SYMPTOMATIC STRICTURING

- Investigator: Hospitalization due to balloon dilatation.

- AbbVie: Event more likely related to pre-existing medical history of constipation due to colon stenosis. Pre-existing Crohn's disease is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ACTIVATED PARTIAL THROMBOPLASTIN TIME: 28 SEC (normal 25.6 to 32.6)

[redacted] 20[redacted] BIOPSY: Not reported

[redacted] **20[redacted] COLONOSCOPY:** No active and immediately perforation noted.

[redacted] **20[redacted] HEMATOCRIT:** 28 % (normal 35.6 to 45.4)

[redacted] **20[redacted] HEMOGLOBIN:** 7.7 G/DL (normal 10.8 to 14.9)

[redacted] **20[redacted] LYMPHOCYTES %:** 24.8 % (normal 21.3 to 50.2)

[redacted] **20[redacted] MCH:** 17.6 PG (normal 26 to 34)

[redacted] **20[redacted] MCV:** 63.9 FL (normal 80 to 100)

[redacted] **20[redacted] PLATELET COUNT:** 340 X10**3/MCL (normal 150 to 361)

[redacted] **20[redacted] POTASSIUM:** 3.6 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] PROTHROMBIN TIME:** 11.1 SEC (normal 9.8 to 11.5)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.38 M/UL (normal 3.78 to 4.99)

[redacted] **20[redacted] SODIUM:** 138 MMOL/L (normal 136 to 145)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3.3 X10**3/MCL (normal 3.54 to 9.06)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

台湾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，症候性結腸狭窄の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，糖尿病，慢性胃炎，下痢，炎症性腸疾患，外痔核，急性胃腸炎，クローン病，結腸狭窄による便秘，非喫煙者及び非飲酒者であった。

投与 441 日後，被験者は症候性結腸狭窄を発現した。

投与 440 日後，被験者は結腸狭窄のため入院した。直腸狭窄及び鉄欠乏性貧血も認められた。被験者はバルーン拡張術を受けた。投与 443 日後，被験者は退院した。

The patient's past medications include:

MEZAVANT XL for CROHN'S DISEASE ([redacted])

PENTASA for CROHN'S DISEASE ([redacted])

ADALIMUMAB for CROHN'S DISEASE ([redacted])

PREDONINE for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

---

1) Colonic stricture (10010005) (Large intestinal stenosis (10074061)) [v.22.0] [10010005]

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 COLON SYMPTOMATIC STRICTURE

- Investigator: HOSPITALIZATION DUE TO BALLOON DILATATION

- AbbVie: Reported event more likely related to Inflammatory Bowel Disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] **COLONOSCOPY:** Crohn's disease with stenosis, status post balloon dilatation.

[redacted] **HEMOGLOBIN:** 7.9 G/DL (normal 11 to 15.2)

[redacted] **PLATELET:** 460 X10**3/MCL (normal 150 to 378)

[redacted] **20[redacted] RED BLOOD CELLS:** 5.25 M/ML (normal 3.78 to 5.25)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4.17 X10**3/MCL (normal 3.25 to 9.16)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-000

台湾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，イレウスの事象を発現した。

Event 3 の臨床経過：

関連する病歴は，慢性胃炎，下痢，炎症性腸疾患，外痔核，急性胃腸炎，クローン病，結腸狭窄による便秘，非喫煙者及び非飲酒者であった。

投与 473 日後，被験者はイレウスを発現した。投与 476 日後，イレウスは消失した。

投与 473 日後，被験者は，間欠性だが進行性の重度の腹痛のため，入院した。被験者は，同時に上気道感染（非重篤）を発現していたため，セフメタゾールによる治療を受けた。臨床検査及び診断法が行われ，CRP 上昇（2.27 mg/dL）が認められた。入院中，発熱は認められなかった。腹痛は改善し始め，便通が認められた。投与 476 日後，被験者は安定した状態を持続していたため，退院した。

The patient's past medications include:

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

PENTASA 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])

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

Causality for RISANKIZUMAB (Blinded)

---

1) Ileus (10021328) (Ileus (10021328)) [v.22.1] [10021328]

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 ILEUS

- Investigator: Not Applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ESR 1HR:** 57 MM/HR (normal 20 to 20)

[redacted] **20[redacted] HEMATOCRIT:** 33.8 % (normal 34.8 to 46.3)

[redacted] **20[redacted] HEMOGLOBIN:** 9.4 G/DL (normal 11.0 to 15.2)

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 2.27 mg/dL (normal 0.1 to 0.3)

[redacted] 20[redacted] KUB ABDOMINAL: Ileus.

[redacted] **20[redacted] KUB ABDOMINAL:** Prominent bowel gas with bowel dilatation, suggestive of ileus. Obscured bilateral psoas muscles.

[redacted] **20[redacted] KUB ABDOMINAL:** CLEAR BILATERAL PSOAS SHADOWS. INCREASED BOWEL GAS IN THE ABDOMEN. NO DEFINITE RADIOPAQUE STONES. NO EVIDENCE OF DESTRUCTIVE BONY LESION AT THE SPINE. MILD SUBCHONDRAL SCLEROSIS AT BILATERAL SACROILIAC JOINTS.

[redacted] **20[redacted] LIPASE:** 9 U/L (normal 11 to 82)

[redacted] **20[redacted] LYMPHOCYTES %:** 10.2 % (normal 18.0 to 48.8)

[redacted] **20[redacted] RDW-CV:** 25.4 % (normal 11.6 to 15.0)

[redacted] **20[redacted] SEGMENT WBC:** 82.2 % (normal 41.6 to 74.4)

[redacted] **20[redacted] SODIUM:** 135 MMOL/L (normal 136 to 145)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.00 X10**3/MCL (normal 3.25 to 9.16)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血	X			
低カリウム血症	X			
口腔真菌感染				X

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

Medical History	Onset Year
DEPRESSION: DEPRESSION SECONDARY TO CROHN'S DISEASE	NOT REPORTED
GASTROESOPHAGEAL REFLUX DISEASE	NOT REPORTED
HEARING DISORDER: MILD HEARING LOSS	NOT REPORTED
HYPERTENSION	NOT REPORTED
OTHER: ALLERGIC RHINITIS	NOT REPORTED
OTHER: DYSPHAGIA	NOT REPORTED
ANEMIA: ANEMIA SECONDARY TO CROHN'S	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: HEADACHE	20[redacted]
OTHER: OCCASIONAL HEADACHES	20[redacted]
INFLAMMATORY BOWEL DISEASE: ILEOCOLIC RESECTION WITH SMALL BOWEL RESECTION	20[redacted]
HYPERLIPIDEMIA: HIGH CHOLESTEROL	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: INTERMITTANT ORAL YEAST INFECTIONS	20[redacted]

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

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 1	[redacted] / 1	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 29	[redacted] / 29	1
M15991 /PLACEBO		INTRAVENOUS	Every 4 Weeks	[redacted] / 62	[redacted] / 62	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 85	[redacted] / 85	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 141	[redacted] / 141	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 197	[redacted] / 197	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 253	[redacted] / 253	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 309	[redacted] / 309	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 363	[redacted] / 363	1
PLACEBO		SUBCUTANEOUS	Every 8 Weeks	[redacted] / 419	[redacted] / 419	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
COLESTIPOL	1 g	QD	Y-M: 20[redacted]
DICYCLOVERINE	10 mg	QID	Y-M: 20[redacted]
CODEINE	600 mg	QD	Y-M: 20[redacted]
DIPHENHYDRAMINE	50 mg	PRN	Y-M: 20[redacted]
FLUTICASONE	200 ug	QD	Y-M: 20[redacted]
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted]
DICYCLOVERINE	10 mg	QD	Y-M: 20[redacted]
LORATADINE	10 mg	BID	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted]
COLECALCIFEROL	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
CARIPRAZINE	3 mg	BID	Y-M: 20[redacted] / -261
NYSTATIN	500000 IU	QID	Y-M: 20[redacted] / 30
ROPINIROLE	0.5 mg	QD	Y-M: 20[redacted] / 32
VORTIOXETINE	10 mg	QD	Y-M: 20[redacted] / 44
PROPOFOL	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 79
PROPOFOL	150 OTHER: UG/KG/MIN	OTHER: CONTINUOUS INFUSION	Y-M: 20[redacted] / 79

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
POTASSIUM	10 mEq	PRN	Y-M: 20[redacted] / 357	Y-M: 20[redacted] / 359
POTASSIUM	20 mEq	QD	Y-M: 20[redacted] / 358	NOT REPORTED

Event #1: Event of Interest - Opportunistic Infections (includes fungal infections)

Event Description	ORAL YEAST INFECTION
Preferred Term	口腔真菌感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 153
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	163
Duration of AE	11 DAYS
Severity	MILD
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	SEVERE ANEMIA
Preferred Term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 356
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 357): Calcium: 2.02 [2.1 - 2.55] MMOL/L; Ery. Mean Corpuscular Hemoglobin: 19.2 [25.6 - 32.2] PG; Ery. Mean Corpuscular Volume: 63.1 [79 - 92.2] FL; Erythrocytes: 3.4 [4.4 - 5.7] 10^12/L; Hematocrit: 0.21 [0.4 - 0.51] FRACTION OF 1; Hemoglobin: 65 [137 - 175] G/L; Leukocytes: 6.3 [4.1 - 10.8] 10^9/L; Platelets: 142 [140 - 370] 10^9/L; Potassium: 3 [3.7 - 5] MMOL/L; Potassium: 2.8 [3.7 - 5] MMOL/L; Sodium: 139 [135 - 143] MMOL/L; [redacted]20[redacted] (Rx Day 358): Potassium: 3.6 [3.7 - 5] MMOL/L; [redacted]20[redacted] (Rx Day 360): Ery. Mean Corpuscular Hemoglobin: 21.9 [25.6 - 32.2] PG; Ery. Mean Corpuscular Volume: 69.2 [79 - 92.2] FL; Erythrocytes: 4.3 [4.4 - 5.7] 10^12/L; Hematocrit: 0.3 [0.4 - 0.51] FRACTION OF 1; Hematocrit: 0.3 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 94 [137 - 175] G/L; Hemoglobin: 94 [137 - 175] G/L; Leukocytes: 4.4 [4.1 - 10.8] 10^9/L; Platelets: 118 [140 - 370] 10^9/L; Potassium: 3.7 [3.7 - 5] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 357): PACKED RED BLOOD CELLS:SATISFACTORY; [redacted]20[redacted] (Rx Day 358): 500 CC PACKED RED BLOOD CELLS:SATISFACTORY; ABDOMINAL CHEST X-RAY:NO ACUTE ABNORMALITIES; [redacted]20[redacted] (Rx Day 359): CAPSULE ENDOSCOPY:NO RESULT; [redacted]20[redacted] (Rx Day 450): COLONOSCOPY:MINIMAL MUCOSAL INFLAMMATION WITH NO ULCERATION. SMALL POLYP NEAR DENTATE LINE

AE Stopped Rx Day	377
Duration of AE	22 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	IDIOPATHIC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

Event #3: Serious Adverse Event

Event Description	HYPOKALEMIA
Preferred Term	低カリウム血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 357
Age at AE Onset	3[redacted]

Laboratory Testing
[redacted]20[redacted] (Rx Day 357): Calcium: 2.02 [2.1 - 2.55] MMOL/L; Ery. Mean Corpuscular Hemoglobin: 19.2 [25.6 - 32.2] PG; Ery. Mean Corpuscular Volume: 63.1 [79 - 92.2] FL; Erythrocytes: 3.4 [4.4 - 5.7] 10^12/L; Hematocrit: 0.21 [0.4 - 0.51] FRACTION OF 1; Hemoglobin: 65 [137 - 175] G/L; Leukocytes: 6.3 [4.1 - 10.8] 10^9/L; Platelets: 142 [140 - 370] 10^9/L; Potassium: 3 [3.7 - 5] MMOL/L; Potassium: 2.8 [3.7 - 5] MMOL/L; Sodium: 139 [135 - 143] MMOL/L; [redacted]20[redacted] (Rx Day 358): Potassium: 3.6 [3.7 - 5] MMOL/L; [redacted]20[redacted] (Rx Day 360): Ery. Mean Corpuscular Hemoglobin: 21.9 [25.6 - 32.2] PG; Ery. Mean Corpuscular Volume: 69.2 [79 - 92.2] FL; Erythrocytes: 4.3 [4.4 - 5.7] 10^12/L; Hematocrit: 0.3 [0.4 - 0.51] FRACTION OF 1; Hematocrit: 0.3 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 94 [137 - 175] G/L; Hemoglobin: 94 [137 - 175] G/L; Leukocytes: 4.4 [4.1 - 10.8] 10^9/L; Platelets: 118 [140 - 370] 10^9/L; Potassium: 3.7 [3.7 - 5] MMOL/L

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (Rx Day 357): PACKED RED BLOOD CELLS:SATISFACTORY; [redacted]20[redacted] (Rx Day 358): 500 CC PACKED RED BLOOD CELLS:SATISFACTORY; ABDOMINAL CHEST X-RAY:NO ACUTE ABNORMALITIES; [redacted]20[redacted] (Rx Day 359): CAPSULE ENDOSCOPY:NO RESULT; [redacted]20[redacted] (Rx Day 450): COLONOSCOPY:MINIMAL MUCOSAL INFLAMMATION WITH NO ULCERATION. SMALL POLYP NEAR DENTATE LINE

AE Stopped Rx Day	360
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CAUSE NOT DOCUMENTED. UNKNOWN.
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

米国の治験責任医師からの報告。本被験者は3[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，重度の貧血及び低カリウム血症の事象を発現した。

Event 2 及び 3 の臨床経過：

関連する病歴は，クローン病に続発した貧血，クローン病，炎症性腸疾患（小腸切除を伴う回腸結腸切除），不眠症，高血圧，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

投与 356 日後，被験者は重度の貧血を発現した。投与 357 日後，被験者は低カリウム血症を発現した。投与 360 日後，低カリウム血症は消失した。投与 377 日後，重度の貧血は消失した。

投与 356 日後，被験者は，ヘモグロビンが 5.8 であったため，入院した。被験者は，数週間疲労，頭部ふらふら感，及び息切れが発現していたと報告した。被験者によると，ほかには何も問題なく，挫傷や吐血はなかった。投与 357 日後及び投与 358 日後，被験者は濃厚赤血球輸血を受けた。低カリウム血症も認められ，治療が必要であった。投与 360 日後，被験者の状態は改善し，被験者は問題ない状態で退院した。

投与された薬剤は，赤血球及び塩化カリウムであった。

The patient's past medications include:

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

Causality for RISANKIZUMAB (Blinded)

---

1) Anemia (10002272) (Anaemia (10002034)) [v.24.0] [10002272]

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

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

Dechallenge: Not Applicable

2) Hypokalemia (10021018) (Hypokalaemia (10021015)) [v.24.0] [10021018]

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 SEVERE ANEMIA

- Investigator: Idiopathic

- AbbVie: The event is more likely related to Crohn's disease with subject having a history of anemia secondary to Crohn's disease since 20[redacted].

Event of HYPOKALEMIA

- Investigator: Cause not documented. Unknown.

- AbbVie: The event is more likely due to underlying Crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL CHEST X-RAY: No acute abnormalities

20[redacted] CAPSULE ENDOSCOPY: No results reported

[redacted] **20[redacted] COLONOSCOPY:** No specific findings of bleeding.

[redacted] **20[redacted] COLONOSCOPY:** Minimal mucosal inflammation with no ulcerations, small polyp near dentate line

[redacted] **20[redacted] ENDOSCOPY:** capsule- no result

[redacted] **20[redacted] HEMATOCRIT:** 21.2 % (normal 40.1 to 51.0)

[redacted] **20[redacted] HEMATOCRIT:** 29.9 % (normal 40.1 to 50.1)

[redacted] **20[redacted] HEMOGLOBIN:** 5.8 G/DL (normal 13.7 to 17.5)

[redacted] **20[redacted] HEMOGLOBIN:** 6.5 G/DL (normal 13.7 to 17.5)

[redacted] **20[redacted] HEMOGLOBIN:** 9.4 G/DL (normal 13.7 to 17.5)

[redacted] **20[redacted] MCH:** 19.2 PG (normal 25.6 to 32.2)

[redacted] **20[redacted] MCV:** 63.1 FL (normal 79 to 92.2)

[redacted] 20[redacted] PHYSICAL EXAMINATION: Non-contributory

[redacted] **20[redacted] PLATELET COUNT:** 118 10^3/ul (normal 140 to 370)

[redacted] **20[redacted] POTASSIUM:** 2.8 MMOL/L (normal 3.7 to 5.0)

[redacted] **20[redacted] POTASSIUM:** 3.6 MMOL/L (normal 3.7 to 5.0)

[redacted] **20[redacted] POTASSIUM:** 3.7 MMOL/L (normal 3.7 to 5.0)

[redacted] **20[redacted] RBC:** 4.31 10^6/ul (normal 4.37 to 5.74)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Oral Fungal Infection: Symptoms not reported.

M15-991 試験

治験の標題： A Multicenter, Randomized, Double-Blind, Placebo Controlled Induction Study to Assess the Efficacy and Safety of Risankizumab in Subjects with Moderately to Severely Active Crohn's Disease Who Failed Prior Biologic Treatment
施設数 / 実施国名： 214 施設 / 40 ヵ国（アルゼンチン，オーストラリア，オーストリア，ベラルーシ，ベルギー，ボスニア・ヘルツェゴヴィナ，ブルガリア，カナダ，チリ，中国，コロンビア，クロアチア，チェコ，デンマーク，エジプト，エストニア，フランス，ドイツ，ギリシャ，アイルランド，イスラエル，イタリア，ラトビア，リトアニア，オランダ，ニュージーランド，ポーランド，ポルトガル，ルーマニア，ロシア連邦，セルビア，シンガポール，スロバキア，南アフリカ，韓国，スペイン，スイス，台湾，イギリス，米国）
治験責任医師： [redacted], MD, FRCPC，他
公表文献 (参考資料) ： なし

治験期間： 最初の被験者の初回来院日：2017 年 12 月 18 日 最後の被験者の最終来院日：2021 年 5 月 19 日	開発のフェーズ：III

治験の種類： 多施設共同，ランダム化，二重盲検，プラセボ対照
目的： 生物学的製剤による前治療で効果不十分又は不耐容であった中等症から重症の活動性クローン病患者を対象に，導入療法としてのリサンキズマブの有効性及び安全性をプラセボと比較して評価する。
被験者数 (計画時と解析時) ： 計画時：579 例 解析時：618 例
診断と主要な組入れ基準： ベースラインの 3 ヵ月以上前にクローン病の確定診断を受けている 18 歳以上 80 歳以下の男女（及び 16 歳以上 18 歳未満で Tanner stage 5 の定義に該当する者）で，ベースライン時のクローン病活動度指数（以下「CDAI」）が 220 以上 450 以下，粘膜炎症の内視鏡的所見においてベースライン時の Simple Endoscopic Score for Crohn's Disease（以下「SES-CD」）が 3 以上（最大 58 例まで），又は小腸大腸型病変若しくは大腸型病変の場合は SES-CD が 6 以上，又は病変が回腸に限局している場合は SES-CD が 4 以上であり，かつ，平均 1 日排便回数（以下「SF」）が 4 回以上及び / 又は平均 1 日腹痛（以下「AP」）スコアが 2 以上の者。
治験方法： 本試験は，中等症から重症の活動性クローン病患者を対象に，導入療法としてのリサンキズマブの有効性及び安全性を評価する，第 III 相，多施設共同，ランダム化，二重盲検，プラセボ対照試験であった。1 剤以上の既承認のクローン病に対する生物学的製剤による前治療で効果不十分又は不耐容であった被験者（以下「Bio-IR」）を本試験に組み入れた。 試験期間は最大 49 週間とし，最大 35 日のスクリーニング期間，12 週導入療法期，投与 12 週時に臨床的改善* を達成しなかった被験者における追加の 12 週間の導入療法期 2，及び治験薬最終投与から 140 日間の追跡調査期とした。ベースライン時，投与 4，8 及び 12 週時又は中止時に臨床評価のための Visit を実施した。投与 12 週時に臨床的改善を達成したすべての被験者が M16-000 試験への組入れに適格となった。投与 12 週時に臨床的改善を達成しなかった被験者は，盲検下で導入療法期 2（投与 12，16 及び 20 週時の追加 Visit，並びに臨床的改善評価のための投与 24 週時 Visit）へ移行した。

* 臨床的改善：平均 1 日 SF が 30%以上減少及び / 又は平均 1 日 AP スコアが 30%以上減少，かついずれもベースラインよりも悪化していない
被験薬，用量，投与方法及びバッチ番号： 12 週導入療法期：盲検下でリサンキズマブ 1200 mg 又は 600 mg を投与 0，4 及び 8 週時に静脈内（以下「IV」）投与した。 導入療法期 2：盲検下でリサンキズマブ 1200 mg を投与 12，16 及び 20 週時に IV 投与した。又は，盲検下でリサンキズマブ 360 mg 又は 180 mg を投与 12 及び 20 週時に皮下（以下「SC」）投与した。 リサンキズマブは，90 mg/mL の溶液として注入用バイアル（バッチ番号：[redacted]）及び 90 mg/mL の注射用プレフィルドシリンジ（バッチ番号：[redacted]）として提供された。
治療期間： 20 週間
対照薬，用量，投与方法及びバッチ番号： 12 週導入療法期：盲検下でプラセボを投与 0，4 及び 8 週時に IV 投与した。 プラセボは，注入用バイアル（バッチ番号：[redacted]）及び注射用プレフィルドシリンジ（バッチ番号：[redacted]）として提供された。
評価基準： 有効性： 米国以外における主要評価項目（co-primary endpoints）は，以下とした。 • 投与 12 週時の臨床的寛解*を達成した被験者の割合 • 投与 12 週時の内視鏡的改善**を達成した被験者の割合 米国における主要評価項目（co-primary endpoints）は，以下とした。 • 投与 12 週時の CDAI に基づく臨床的寛解（以下「臨床的 CDAI 寛解」）***を達成した被験者の割合 • 投与 12 週時の内視鏡的改善を達成した被験者の割合 米国以外における順位付けされた副次評価項目は，以下とした。 1. 投与 12 週時の臨床的 CDAI 寛解を達成した被験者の割合 2. 投与 4 週時の CDAI に基づく臨床的改善（以下「臨床的 CDAI 改善」）を達成した被験者の割合 3. 投与 4 週時の臨床的寛解を達成した被験者の割合 4. 投与 12 週時の臨床的 CDAI 改善を達成した被験者の割合 5. 投与 12 週時の慢性疾患治療-疲労の機能評価（以下「FACIT-F」）のベースラインからの平均変化量 6. 投与 12 週時の炎症性腸疾患質問票（以下「IBDQ」）トータルスコアのベースラインからの平均変化量 7. 投与 12 週時の高度臨床的改善かつ内視鏡的改善を達成した被験者の割合 8. 投与 12 週時の内視鏡的寛解を達成した被験者の割合 9. 投与 4 週時の高度臨床的改善を達成した被験者の割合 10. 投与 12 週時の内視鏡的治癒（潰瘍が治癒した状態）を達成した被験者の割合 11. 投与 12 週時の高度臨床的改善を達成した被験者の割合 12. ベースライン時にいずれかの腸管外合併症（以下「EIMs」）を有していた被験者のうち，投与 12 週時の EIMs の消失を達成した被験者の割合 13. 投与 12 週時までのクローン病関連で入院した被験者の割合 14. ベースライン時に排液性瘻孔を有していた被験者のうち，投与 12 週時の排液性瘻孔なしを達成した被験者の割合 15. 投与 12 週時のクローン病患者の仕事の生産性及び活動障害に関する質問票（以下「WPAI-CD」）総労働損

失のベースラインからの変化量

16. 投与 12 週時の SF-36 健康調査票（以下「SF-36」）身体的側面の生活の質（以下「QoL」）サマリー（PCS）スコアのベースラインからの変化量

米国における順位付けされた副次評価項目は，以下とした。

1. 投与 12 週時の臨床的寛解を達成した被験者の割合
2. 投与 4 週時の臨床的 CDAI 改善を達成した被験者の割合
3. 投与 12 週時の臨床的 CDAI 改善を達成した被験者の割合
4. 投与 12 週時の FACIT-F のベースラインからの平均変化量
5. 投与 4 週時の臨床的 CDAI 寛解を達成した被験者の割合
6. 投与 12 週時の臨床的 CDAI 改善かつ内視鏡的改善を達成した被験者の割合
7. 投与 12 週時の SF 寛解を達成した被験者の割合
8. 投与 12 週時の AP 寛解を達成した被験者の割合
9. 投与 12 週時の内視鏡的寛解を達成した被験者の割合
10. 投与 4 週時の高度臨床的改善を達成した被験者の割合
11. 投与 12 週時の内視鏡的治癒（潰瘍が治癒した状態）を達成した被験者の割合
12. 投与 12 週時の高度臨床的改善を達成した被験者の割合
13. ベースライン時にいずれかの EIMs を有していた被験者のうち，投与 12 週時の EIMs の消失を達成した被験者の割合
14. 投与 12 週時までのクローン病関連で入院した被験者の割合
15. ベースライン時に排液性瘻孔を有していた被験者のうち，投与 12 週時の排液性瘻孔なしを達成した被験者の割合

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

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

*** 臨床的 CDAI 寛解：CDAI スコアが 150 未満

薬物動態及び免疫原性：

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

安全性：

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

統計手法：

有効性：

Co-primary endpoints について，intent-to-treat（以下「ITT」）1A 解析対象集団（12 週導入療法期の ITT 解析対象集団のうち，ベースラインの SES-CD が 6 以上［病変が回腸に限局している場合は SES-CD が 4 以上］の被験者）において，リサンキズマブ 600 mg IV 群及び 1200 mg IV 群の各群とプラセボ群間で，ランダム化時の層別因子（過去に無効であった生物学的製剤の数［1 以下，1 超］及びベースラインのステロイド使用の有無［はい，いいえ］）で調整した Cochran-Mantel-Haenszel（以下「CMH」）検定を用いて解析した。投与群間差の両側 95%信頼区間を CMH に基づき算出した。有効性の co-primary endpoints では，補足的な解析として欠測値を補完しない as observed（AO）データを用いた CMH 検定を実施した。この解析は ITT1A 解析対象集団を用いて実施した。

連続変数で表される反復測定した有効性の副次評価項目は，一般的に，反復測定混合効果モデル（以下「MMRM」）を用いて解析した。このモデルには，投与群，Visit，Visit と投与群の交互作用，及びランダム化

時の層別因子を固定効果（カテゴリー変数），ベースライン値を固定共変量（連続変数）として含めた。
MMRM 解析は主に推測目的とみなした。連続変数で表される有効性の副次評価項目のうち，治験薬投与後では 1 時点でのみ収集すると規定された項目については，コロナウイルス感染症（COVID-19）による欠測データに多重補完法（MI）を用いた共分散分析を用いて解析した（ANCOVA-C）。
カテゴリー変数で表される有効性の副次評価項目は，排液性瘻孔及びクローン病関連の入院についての評価項目を除いて，層別因子（過去に無効であった生物学的製剤の数［1 以下，1 超］及びベースラインのステロイド使用の有無［はい，いいえ］）で調整した CMH 検定を用いて解析した。CMH を用いてリサンキズマブ各群とプラセボ群の投与群間差の両側 95%信頼区間を算出した。「ベースライン時に排液性瘻孔を有していた被験者のうち，投与 12 週時の排液性瘻孔なしの達成」及び「投与 12 週時までのクローン病関連の入院の発生」の評価項目は，カイ二乗検定（又は分割表において 20%以上のセルで期待度数が 5 未満となる場合にはフィッシャーの正確検定）を用いて解析した。

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

安全性：
有害事象及び治験薬と関連ありの有害事象の発現割合，バイタルサインの変化量，身体検査結果，及び臨床検査値を解析した。

内訳

12 週導入療法期では，618 例（リサンキズマブ 600 mg IV 群 206 例，1200 mg IV 群 205 例，プラセボ群 207 例）がランダム化され，治験薬を投与された。このうち，投与 12 週時までの治験薬の投与を完了した被験者の割合は，リサンキズマブ 600 mg IV 群及び 1200 mg IV 群でプラセボ群と比較して高かった（リサンキズマブ 600 mg IV 群 98.1%，1200 mg IV 群 97.1%，プラセボ群 89.9%）。

導入療法期 2 では，投与 12 週時に臨床的改善を達成しなかった被験者のうち，12 週導入療法期にリサンキズマブ IV 投与を受けた被験者を，リサンキズマブ 1200 mg IV 群，360 mg SC 群及び 180 mg SC 群のいずれかに 1:1:1 の比でランダム化し，12 週導入療法期にプラセボ投与を受けた被験者はリサンキズマブ 1200 mg IV 投与を受けた。211 例が組み入れられ，リサンキズマブ 180 mg SC 群 41 例，360 mg SC 群 42 例，1200 mg IV 群 42 例がランダム化され，86 例はランダム化されずに，プラセボ / リサンキズマブ 1200 mg IV 群に割り付けられ，治験薬を投与された。治験薬の投与を完了した被験者の割合は全体で 91.0%であり，投与群間でおおむね均衡していた。

有効性の結果

リサンキズマブ 600 mg IV 群及び 1200 mg IV 群で，プラセボ群と比較したとき，米国以外の co-primary endpoints である投与 12 週時の臨床的寛解及び内視鏡的改善，米国の co-primary endpoints である投与 12 週時の臨床的 CDAI 寛解及び内視鏡的改善のいずれもが達成された。投与 12 週時の臨床的寛解（米国以外）又は臨床的 CDAI 寛解（米国）を達成した被験者の割合は，リサンキズマブ 600 mg IV 群（臨床的寛解 34.6%，臨床的 CDAI 寛解 42.0%，以下同順）及び

1200 mg IV 群（39.8%，40.3%）でプラセボ群（19.3%，19.8%）と比較して統計学的に有意に高かった（$P \leq 0.001$）。投与 12 週時の内視鏡的改善を達成した被験者の割合は，リサンキズマブ 600 mg IV 群（28.8%）及び 1200 mg IV 群（34.2%）でプラセボ群（11.2%）と比較して統計学的に有意に高かった（$P < 0.001$）。全体として，リサンキズマブ 600 mg IV 群と 1200 mg IV 群で数値的に同様の結果であった。

全体として，リサンキズマブ各群でプラセボ群と比較して，クローン病の徴候及び症状の消失，QoL の改善，粘膜炎症の内視鏡的所見の減少，並びにクローン病関連の入院の減少について明確な効果が示された。米国以外及び米国の評価項目のほとんどについて，リサンキズマブ各群でプラセボ群と比較して統計学的に有意な差が認められた。全体として，リサンキズマブ 600 mg IV 群と 1200 mg IV 群で数値的に同様の結果であった。

クローン病の徴候及び症状の改善（臨床的 CDAI 寛解，臨床的寛解，平均 1 日 AP スコア，AP 寛解，平均 1 日 SF，SF 寛解，臨床的 CDAI 改善，臨床的改善，高度臨床的改善，クローン病症状重症度［CSS］，EIMs の消失，変化に関する患者の全体的印象［PGIC］及び重症度に関する患者の全体的印象［PGIS］の経時的変化），並びに QoL の改善（IBDQ，FACIT-F，WPAI-CD，European Quality of Life 5 Dimensions 5 Levels［EQ-5D-5L］，及び SF-36 スコア）が，リサンキズマブ各群でプラセボ群と比較して経時的に示された。更に，投与 12 週時の便中カルプロテクチン（FCP），高感度 C 反応性蛋白（以下「hs-CRP」），及び SES-CD のベースラインからの変化量は，リサンキズマブ各群でプラセボ群と比較して大きかった。

投与 12 週時に臨床的改善を達成しなかった被験者では，投与 24 週時の臨床的改善を達成した被験者の割合は高く，各投与群で数値的に同様であった（リサンキズマブ 180 mg SC 群 76.7%，360 mg SC 群 75.9%，1200 mg IV 群 61.5%，プラセボ / リサンキズマブ 1200 mg IV 群 81.0%）。

薬物動態及び免疫原性の結果

本試験開始から 12 週間のリサンキズマブ導入療法を受けた被験者では，血清中リサンキズマブ濃度の推移は 600 mg と 1200 mg の用量間でおおむね用量比例関係が示された。投与 12 週時のトラフ濃度は，リサンキズマブ 600 mg IV では 34.8 µg/mL，1200 mg IV では 65.1 µg/mL であった。投与 12 週時に臨床的改善を達成せず，導入療法期 2 にリサンキズマブの投与を受けた被験者では，投与 24 週時の血清中リサンキズマブ濃度の幾何平均値はおおむね用量に依存し，投与量が高いほど血清中リサンキズマブ濃度が高かった。

二重盲検下の 12 週導入療法期に，リサンキズマブの導入療法を受けた評価可能な被験者のうち，治験薬投与に起因する抗薬物抗体の発現率は約 1.5%（6/397 例），中和抗体が陽性であった被験者は 1 例（0.3%）であった。投与 12 週時に臨床的改善を達成した被験者と臨床的改善を達成しなかった被験者で，投与 12 週時までの抗薬物抗体の発現率はおおむね同様であった。導入療法期 2 を含む投与 0 週時から投与 24 週時の間に，投与 12 週時に臨床的改善を達成せず，導入療法期 2 にリサンキズマブを投与された評価可能な被験者のうち，治験薬投与に起因する抗薬物抗体の発現率は約 1.6%（3/193 例）であった。抗薬物抗体が陽性であったこれらの被験者のうち，中和抗体が陽性であった被験者はいなかった。治験薬投与に起因する抗薬物抗体の最初

の発現までの期間は，リサンキズマブの初回投与から 4.14–7.57 週後であった。リサンキズマブを投与された被験者の抗薬物抗体の抗体価は，試験期間を通して 10–83 であった。

安全性の結果

12 週導入療法期の有害事象の発現割合は，プラセボ群で数値的に高かった（リサンキズマブ 600 mg IV 群 47.6%，1200 mg IV 群 59.0%，プラセボ群 66.2%，以下同順）。重篤な有害事象，高度の有害事象，及び治験薬の投与中止に至った有害事象の発現割合は，プラセボ群で数値的に高く，ほとんどが原疾患に起因するものと考えられた。リサンキズマブ 1200 mg IV 群で治験薬を 1 回投与された 1 例が死亡したが，当該被験者は悪性腫瘍（肺の扁平上皮癌）を有しており，死亡は，治験責任（分担）医師及び治験依頼者により治験薬と関連なしと判断された。リサンキズマブ各群で発現割合が高かった有害事象は，頭痛（5.3%，4.9%，5.3%），関節痛（3.9%，4.4%，4.3%），及び上咽頭炎（3.9%，3.9%，5.3%）であり，発現割合はプラセボ群と同様であった。特に注目すべき事象の発現割合は，重篤な感染症を除いて投与群間で同様であった。重篤な感染症の発現割合はプラセボ群で数値的に高く，主にプラセボ群の被験者で認められた原疾患に起因するものと考えられた。いずれの投与群でも，活動性結核，委員会判定されたアナフィラキシー反応，重篤なアナフィラキシー反応，重篤な過敏症，非黒色腫皮膚癌（以下「NMSC」），委員会判定された主要心血管イベント（以下「MACE」），及び委員会判定された Extended MACE は認められなかった。過敏症の有害事象の発現割合はリサンキズマブ 1200 mg IV 群でプラセボ群と比較して数値的に高かったが，リサンキズマブ 600 mg IV 群ではプラセボ群と比較して数値的に低かった。全体として，過敏症反応の発現割合はリサンキズマブ各群とプラセボ群で同様であった。注射部位反応（注入に伴う反応を含む）の発現割合は投与群間で同様であり，いずれの事象も軽度又は中等度で，治験薬の投与中止に至った事象は認められなかった。注射部位反応（注入に伴う反応を含む）の事象はおおむね過敏症反応を示唆するものではなかった。リサンキズマブ各群では，日和見感染及び帯状疱疹は認められなかった。肝関連事象の発現割合は低く，投与群間で同様であり，すべて肝酵素上昇であった。投与群間での肝関連事象，臨床検査値及び外れ値の解析の包括的な評価から，肝障害に関する安全性の問題は認められなかった。臨床的に意義があると判断した臨床検査値及びバイタルサインの基準に該当した被験者の割合は低く，投与群間で同様であった。

リサンキズマブ 180 mg SC，360 mg SC，又は 1200 mg IV 投与による継続投与は，おおむね安全で忍容性は良好であった。新たな安全性のリスクは特定されず，追加の 12 週間の導入療法による安全性プロファイルの悪化は認められなかった。全体として安全性プロファイルは，リサンキズマブの既知の安全性プロファイルと一致していた。導入療法期 2 では，有害事象全体の発現割合は投与群間で同様であった（リサンキズマブ 180 mg SC 群 46.3%，360 mg SC 群 47.6%，1200 mg IV 群 57.1%，プラセボ / リサンキズマブ 1200 mg IV 群 50.0%，以下同順）。重篤な有害事象，高度の有害事象，及び治験薬の投与中止に至った有害事象を発現した被験者の割合は低く，投与群間でおおむね同様であった。追跡調査期間（140 日間）中，リサンキズマブ 1200 mg IV 群の 1 例が死亡し，当該被験者では治験薬の最終投与から 130 日後に敗血症が認められ，ク

ローン病の増悪が原因と考えられた。本事象は治験責任（分担）医師及び治験依頼者により治験薬と関連なしと判断された。リサンキズマブ群全体で発現割合が高かった有害事象は，クローン病（2.4%，0%，9.5%，5.8%），腹痛（7.3%，2.4%，4.8%，3.5%），関節痛（4.9%，2.4%，2.4%，5.8%），頭痛（2.4%，2.4%，7.1%，4.7%），及び発熱（7.3%，4.8%，4.8%，2.3%）であった。特に注目すべき事象の発現割合は，重篤な感染症を含めて低かった。委員会判定された MACE，委員会判定された Extended MACE，活動性結核，悪性腫瘍，悪性腫瘍（NMSC を除く），NMSC，重篤な過敏症，委員会判定されたアナフィラキシー反応，重篤なアナフィラキシー反応は認められなかった。過敏症の有害事象はいずれも非重篤で，軽度又は中等度であり，治験薬の投与中止には至らなかった。注射部位反応の事象はいずれも非重篤で，軽度であり，投与の変更はなかった。注射部位反応の事象はおおむね過敏症反応を示唆するものではなかった。日和見感染は 2 件報告された。肝関連事象の発現割合は低く，臨床検査値異常を示していた。肝関連事象はいずれも非重篤で，軽度又は中等度であり，治験薬と関連なしと判断され，治験薬投与の中断又は中止には至らなかった。投与群間の肝関連事象，臨床検査値及び外れ値の解析の包括的な評価から，肝障害に関する安全性の問題は認められなかった。臨床的に意義があると判断した臨床検査値及びバイタルサインの基準に該当した被験者の割合は低く，投与群間で同様であった。

結論

本試験の co-primary endpoints である投与 12 週時の臨床的寛解（米国以外）又は臨床的 CDAI 寛解（米国）及び投与 12 週時の内視鏡的改善が達成された。

全体として，治療抵抗性の患者集団において，リサンキズマブ 600 mg IV 又は 1200 mg IV 投与の導入療法により，クローン病の徴候及び症状，QoL，並びに内視鏡的評価の改善がプラセボと比較して統計学的に有意に高い割合で認められ，米国及び米国以外のほとんどの副次評価項目について，リサンキズマブ各群でプラセボ群と比較して統計学的に有意な差が認められた。投与 4 週時の臨床的 CDAI 改善，高度臨床的改善，臨床的 CDAI 寛解及び臨床的寛解を達成した被験者の割合は，リサンキズマブ各群でプラセボ群と比較して高く，ほとんどの評価項目について，この早期の評価時点で統計学的に有意な差が認められた。投与 4，8 及び投与 12 週時の hs-CRP の減少量の平均値は，リサンキズマブ 600 mg IV 群及び 1200 mg IV 群でプラセボ群と比較して大きかった（名目 P 値≤ 0.001）。

導入療法期 2 の結果から，12 週間のリサンキズマブ IV 投与の導入療法により臨床的改善を達成しなかった被験者に，SC 又は IV 投与により，リサンキズマブを継続投与したとき，投与 24 週時の臨床的改善を達成した被験者の割合は高かった。導入療法期 2 からリサンキズマブ IV 投与を開始した被験者では，12 週導入療法期における 12 週間の IV 投与後と同様の結果が認められた。

リサンキズマブ 600 mg IV 群及び 1200 mg IV 群で，血清中トラフ濃度の幾何平均値は 12 週導入療法期を通しておおむね用量比例関係が示された。導入療法期 2 の投与 24 週時のリサンキズマブの曝露量は，おおむね用量に依存していた。抗薬物抗体及び / 又は中和抗体を発現した被験

者数は限られており，リサンキズマブの曝露量に及ぼす免疫原性の明らかな影響は認められなかった。

リサンキズマブ 600 mg IV 又は 1200 mg IV 投与の 12 週導入療法，及びリサンキズマブ 180 mg SC，360 mg SC，又は 1200 mg IV 投与の追加の 12 週間の継続療法は，おおむね安全で忍容性は良好であった。新たな安全性のリスクは特定されず，全体として安全性プロファイルは，リサンキズマブの既知の安全性プロファイルと一致していた。

本試験の曝露状況の概要及び本試験で発現した有害事象を以下のとおり示す。

項目	12 週導入療法期 （SA1）	導入療法期 2 （SA2）
曝露状況の概要	表 1	表 2
有害事象の概要	表 3	表 4
すべての有害事象	表 5	表 6
死亡に至った有害事象	表 7	表 8
重篤な有害事象	表 9	表 10

表1

[redacted]20[redacted] 14:13 <[redacted]>
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL

TABLE 14.1__1.20.2

Extent of Exposure for the 12-Week Induction Period
(SA1 Population)

Exposure to study drug	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Total (N=618) n (%)
Duration interval (days)				
1 - 28	12 (5.8)	2 (1.0)	3 (1.5)	17 (2.8)
29 - 56	7 (3.4)	0	3 (1.5)	10 (1.6)
57 - 84	130 (62.8)	127 (61.7)	140 (68.3)	397 (64.2)
85 - 112	58 (28.0)	77 (37.4)	58 (28.3)	193 (31.2)
> 112	0	0	1 (0.5)	1 (0.2)
Duration (days)				
N	207	206	205	618
Mean (SD)	79.5 (14.61)	83.7 (7.26)	83.0 (9.80)	82.0 (11.13)
MEDIAN	84.0	84.0	84.0	84.0
Min, Max	28, 106	28, 108	28, 154	28, 154

Note: SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Total exposure is defined as last dose date of study drug in induction period + 28 - first dose date of study drug, first dose date of study drug in induction period 2, if applicable - first dose date of study drug, or first dose date of study drug in M16-000, if applicable - first dose date of study drug, whichever is shorter.

Program Source Code: [redacted]

表2

[redacted]20[redacted] 14:13 <[redacted]>
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL

TABLE 14.1__2.7

Extent of Exposure for the Induction Period 2
(SA2 Population)

Exposure to study drug	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
Duration interval (days)					
1 - 28	0	0	1 (2.4)	5 (5.8)	6 (2.8)
29 - 56	0	2 (4.8)	2 (4.8)	3 (3.5)	7 (3.3)
57 - 84	18 (43.9)	17 (40.5)	28 (66.7)	57 (66.3)	120 (56.9)
85 - 112	19 (46.3)	19 (45.2)	11 (26.2)	21 (24.4)	70 (33.2)
> 112	4 (9.8)	4 (9.5)	0	0	8 (3.8)
Duration (days)					
N	41	42	42	86	211
Mean (SD)	93.2 (13.95)	89.3 (13.93)	79.5 (13.14)	77.9 (14.50)	83.5 (15.32)
MEDIAN	88.0	85.5	84.0	83.0	84.0
Min, Max	76, 124	56, 118	28, 111	28, 92	28, 124

Note: SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Total exposure is defined as last dose date of study drug in induction period 2 + 28 [for IV dose] or 56 [for SC dose] - first dose date of study drug in induction period 2 , first dose date of study drug in M16-000, if applicable - first dose date of study drug in Induction Period 2, whichever is shorter.

Program Source Code: [redacted]

表3

[redacted]20[redacted] 14:14 <[redacted]>
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__1.1.1.5

Overview of Treatment-Emergent Adverse Events and All Deaths
during the 12-Week Induction Period
(SA1 Population)

		-------- Risankizumab ----------			- 95% CI& for Treatment Difference -	
	Placebo IV (N=207) n (%)	600 mg IV (N=206) n (%)	1200 mg IV (N=205) n (%)	Total (N=411) n (%)	600 mg IV VS Placebo IV	1200 mg IV VS Placebo IV
Subjects with any treatment-emergent						
Adverse event (AE)	137 (66.2)	98 (47.6)	121 (59.0)	219 (53.3)	-18.6 (-28.0, -9.2)	-7.2 (-16.5, 2.2)
AE related to COVID-19	1 (0.5)	0	0	0	-0.5 (-1.4, 0.5)	-0.5 (-1.4, 0.5)
AE related to study drug according to the investigator	45 (21.7)	27 (13.1)	39 (19.0)	66 (16.1)	-8.6 (-15.9, -1.4)	-2.7 (-10.5, 5.1)
Severe AE	25 (12.1)	7 (3.4)	12 (5.9)	19 (4.6)	-8.7 (-13.8, -3.6)	-6.2 (-11.7, -0.7)
Serious AE	26 (12.6)	10 (4.9)	9 (4.4)	19 (4.6)	-7.7 (-13.1, -2.3)	-8.2 (-13.5, -2.9)
AE leading to discontinuation of study drug	17 (8.2)	2 (1.0)	5 (2.4)	7 (1.7)	-7.2 (-11.2, -3.3)	-5.8 (-10.1, -1.5)
AE leading to death	0	0	1 (0.5)	1 (0.2)	0.0	0.5 (-0.5, 1.4)
All deaths						
Deaths occurring <= 140 days after last dose of study drug	0	0	1 (0.5)	1 (0.2)	0.0	0.5 (-0.5, 1.4)
Deaths occurring > 140 days after last dose of study drug	0	0	0	0	0.0	0.0
Deaths related to COVID-19	0	0	0	0	0.0	0.0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.
& 95% CI for treatment difference is based on the normal approximation.

Program Source Code: [redacted]

表4

[redacted]20[redacted] 14:14 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__1.2.1.1

Overview of Treatment-Emergent Adverse Events and All Deaths
during the Induction Period 2
(SA2 Population)

	Risankizumab			Placebo IV/ Risankizumab	
	180 mg SC (N=41) n (%)	360 mg SC (N=42) n (%)	1200 mg IV (N=42) n (%)	1200 mg IV (N=86) n (%)	Total (N=211) n (%)
Subjects with any treatment-emergent					
Adverse event (AE)	19 (46.3)	20 (47.6)	24 (57.1)	43 (50.0)	106 (50.2)
AE related to COVID-19	0	0	0	2 (2.3)	2 (0.9)
AE related to study drug according to the investigator	7 (17.1)	11 (26.2)	4 (9.5)	17 (19.8)	39 (18.5)
Severe AE	2 (4.9)	0	2 (4.8)	6 (7.0)	10 (4.7)
Serious AE	2 (4.9)	2 (4.8)	3 (7.1)	9 (10.5)	16 (7.6)
AE leading to discontinuation of study drug	1 (2.4)	1 (2.4)	1 (2.4)	1 (1.2)	4 (1.9)
AE leading to death	0	0	1 (2.4)	0	1 (0.5)
All deaths					
Deaths occurring <= 140 days after last dose of study drug	0	0	1 (2.4)	0	1 (0.5)
Deaths occurring > 140 days after last dose of study drug	0	0	0	0	0
Deaths related to COVID-19	0	0	0	0	0

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表5

[redacted]20[redacted] 14:14 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
Any adverse event	137 (66.2)	98 (47.6)	121 (59.0)	219 (53.3)
血液およびリンパ系障害	16 (7.7)	8 (3.9)	8 (3.9)	16 (3.9)
貧血	11 (5.3)	5 (2.4)	6 (2.9)	11 (2.7)
骨髄機能不全	1 (0.5)	0	0	0
好酸球増加症	0	1 (0.5)	0	1 (0.2)
鉄欠乏性貧血	1 (0.5)	0	1 (0.5)	1 (0.2)
白血球増加症	0	0	1 (0.5)	1 (0.2)
白血球減少症	1 (0.5)	1 (0.5)	0	1 (0.2)
リンパ球減少症	2 (1.0)	1 (0.5)	0	1 (0.2)
骨髄抑制	1 (0.5)	0	0	0
好中球増加症	0	1 (0.5)	0	1 (0.2)
血小板増加症	1 (0.5)	0	0	0
心臓障害	1 (0.5)	1 (0.5)	3 (1.5)	4 (1.0)
心房細動	0	0	2 (1.0)	2 (0.5)
心房粗動	0	1 (0.5)	0	1 (0.2)
冠動脈疾患	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
心臓障害 (Cont.)				
動悸	0	0	1 (0.5)	1 (0.2)
耳および迷路障害	1 (0.5)	0	2 (1.0)	2 (0.5)
回転性めまい	1 (0.5)	0	1 (0.5)	1 (0.2)
頭位性回転性めまい	0	0	1 (0.5)	1 (0.2)
内分泌障害	1 (0.5)	0	1 (0.5)	1 (0.2)
クッシング様症状	1 (0.5)	0	1 (0.5)	1 (0.2)
眼障害	4 (1.9)	4 (1.9)	1 (0.5)	5 (1.2)
白内障	0	1 (0.5)	0	1 (0.2)
ドライアイ	0	1 (0.5)	0	1 (0.2)
上強膜炎	1 (0.5)	0	0	0
眼脂	0	1 (0.5)	0	1 (0.2)
眼痛	1 (0.5)	0	1 (0.5)	1 (0.2)
眼そう痒症	1 (0.5)	0	0	0
流涙増加	0	1 (0.5)	0	1 (0.2)
視力障害	1 (0.5)	0	0	0
胃腸障害	71 (34.3)	34 (16.5)	33 (16.1)	67 (16.3)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
胃腸障害 (Cont.)				
腹部不快感	0	1 (0.5)	0	1 (0.2)
腹部膨満	2 (1.0)	2 (1.0)	1 (0.5)	3 (0.7)
腹部腫瘤	2 (1.0)	1 (0.5)	1 (0.5)	2 (0.5)
腹痛	11 (5.3)	5 (2.4)	3 (1.5)	8 (1.9)
下腹部痛	2 (1.0)	0	0	0
上腹部痛	2 (1.0)	4 (1.9)	3 (1.5)	7 (1.7)
腹部圧痛	0	0	1 (0.5)	1 (0.2)
裂肛	4 (1.9)	0	0	0
痔瘻	3 (1.4)	3 (1.5)	2 (1.0)	5 (1.2)
肛門失禁	0	0	2 (1.0)	2 (0.5)
肛門括約筋無緊張症	1 (0.5)	0	0	0
肛門狭窄	0	0	1 (0.5)	1 (0.2)
肛門直腸障害	1 (0.5)	0	0	0
アフタ性潰瘍	3 (1.4)	1 (0.5)	2 (1.0)	3 (0.7)
大腸炎	0	0	2 (1.0)	2 (0.5)
便秘	2 (1.0)	2 (1.0)	1 (0.5)	3 (0.7)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
胃腸障害 (Cont.)				
クローン病	33 (15.9)	8 (3.9)	4 (2.0)	12 (2.9)
下痢	2 (1.0)	3 (1.5)	2 (1.0)	5 (1.2)
口内乾燥	0	1 (0.5)	1 (0.5)	2 (0.5)
細菌叢異常	1 (0.5)	0	0	0
消化不良	5 (2.4)	2 (1.0)	3 (1.5)	5 (1.2)
嚥下障害	1 (0.5)	0	1 (0.5)	1 (0.2)
小腸炎	1 (0.5)	0	0	0
腸炎	1 (0.5)	0	0	0
食中毒	1 (0.5)	0	0	0
排便回数増加	1 (0.5)	1 (0.5)	0	1 (0.2)
胃食道逆流性疾患	1 (0.5)	0	1 (0.5)	1 (0.2)
血便排泄	1 (0.5)	1 (0.5)	2 (1.0)	3 (0.7)
痔核	3 (1.4)	0	0	0
回腸狭窄	1 (0.5)	0	0	0
イレウス	0	1 (0.5)	0	1 (0.2)
麻痺性イレウス	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
胃腸障害 (Cont.)				
大腸狭窄	0	1 (0.5)	0	1 (0.2)
大腸潰瘍	0	1 (0.5)	0	1 (0.2)
大腸ポリープ	0	0	1 (0.5)	1 (0.2)
悪心	11 (5.3)	5 (2.4)	3 (1.5)	8 (1.9)
嚥下痛	0	1 (0.5)	0	1 (0.2)
食道潰瘍	1 (0.5)	0	0	0
口腔粘膜水疱形成	1 (0.5)	0	0	0
口腔内痛	0	1 (0.5)	0	1 (0.2)
直腸炎	1 (0.5)	0	0	0
直腸分泌物	1 (0.5)	0	0	0
直腸出血	1 (0.5)	1 (0.5)	0	1 (0.2)
小腸閉塞	2 (1.0)	1 (0.5)	0	1 (0.2)
小腸潰瘍	1 (0.5)	0	0	0
スピゲリウスヘルニア	1 (0.5)	0	0	0
口内炎	1 (0.5)	0	0	0
亜イレウス	0	0	1 (0.5)	1 (0.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
胃腸障害 (Cont.)				
歯痛	0	2 (1.0)	1 (0.5)	3 (0.7)
嘔吐	4 (1.9)	3 (1.5)	3 (1.5)	6 (1.5)
一般・全身障害および投与部位の状態	25 (12.1)	11 (5.3)	16 (7.8)	27 (6.6)
無力症	1 (0.5)	1 (0.5)	4 (2.0)	5 (1.2)
胸痛	0	0	1 (0.5)	1 (0.2)
悪寒	2 (1.0)	0	0	0
不快感	0	1 (0.5)	0	1 (0.2)
疲労	8 (3.9)	4 (1.9)	3 (1.5)	7 (1.7)
炎症	1 (0.5)	0	0	0
インフルエンザ様疾患	2 (1.0)	2 (1.0)	0	2 (0.5)
注入部位内出血	0	0	1 (0.5)	1 (0.2)
注入部位血管外漏出	0	0	1 (0.5)	1 (0.2)
注入部位疼痛	1 (0.5)	0	0	0
注入部位腫脹	1 (0.5)	1 (0.5)	0	1 (0.2)
注射部位疼痛	0	0	1 (0.5)	1 (0.2)
浮腫	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
末梢性浮腫	2 (1.0)	0	1 (0.5)	1 (0.2)
疼痛	0	0	1 (0.5)	1 (0.2)
骨盤腔内腫瘤	0	0	1 (0.5)	1 (0.2)
末梢腫脹	1 (0.5)	0	0	0
発熱	9 (4.3)	4 (1.9)	3 (1.5)	7 (1.7)
肝胆道系障害	0	1 (0.5)	0	1 (0.2)
胆管狭窄	0	1 (0.5)	0	1 (0.2)
免疫系障害	5 (2.4)	0	4 (2.0)	4 (1.0)
薬物過敏症	0	0	2 (1.0)	2 (0.5)
食物アレルギー	1 (0.5)	0	0	0
過敏症	1 (0.5)	0	0	0
季節性アレルギー	3 (1.4)	0	2 (1.0)	2 (0.5)
感染症および寄生虫症	51 (24.6)	31 (15.0)	37 (18.0)	68 (16.5)
腹部膿瘍	1 (0.5)	0	0	0
四肢膿瘍	1 (0.5)	0	0	0
ダニ皮膚炎	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
感染症および寄生虫症 (Cont.)				
肛門膿瘍	3 (1.4)	0	1 (0.5)	1 (0.2)
真菌性肛門感染	0	0	2 (1.0)	2 (0.5)
体部白癬	0	1 (0.5)	0	1 (0.2)
気管支炎	2 (1.0)	2 (1.0)	2 (1.0)	4 (1.0)
COVID－19	1 (0.5)	0	0	0
男性外性器蜂巣炎	1 (0.5)	0	0	0
クロストリジウム・ディフィシレ感染	1 (0.5)	0	0	0
結膜炎	0	1 (0.5)	0	1 (0.2)
膀胱炎	0	1 (0.5)	0	1 (0.2)
サイトメガロウイルス性大腸炎	1 (0.5)	0	0	0
耳感染	1 (0.5)	0	1 (0.5)	1 (0.2)
大腸菌性尿路感染	1 (0.5)	0	0	0
毛包炎	0	0	1 (0.5)	1 (0.2)
胃腸炎	4 (1.9)	0	1 (0.5)	1 (0.2)
大腸菌性胃腸炎	0	0	1 (0.5)	1 (0.2)
ウイルス性胃腸炎	0	0	2 (1.0)	2 (0.5)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
感染症および寄生虫症 (Cont.)				
消化管感染	1 (0.5)	0	0	0
真菌性性器感染	0	0	1 (0.5)	1 (0.2)
単純ヘルペス	1 (0.5)	0	0	0
帯状疱疹	1 (0.5)	0	0	0
麦粒腫	0	0	1 (0.5)	1 (0.2)
感染性瘻孔	1 (0.5)	0	0	0
インフルエンザ	1 (0.5)	3 (1.5)	3 (1.5)	6 (1.5)
喉頭炎	0	1 (0.5)	0	1 (0.2)
下気道感染	1 (0.5)	0	1 (0.5)	1 (0.2)
上咽頭炎	11 (5.3)	8 (3.9)	8 (3.9)	16 (3.9)
好中球減少性敗血症	1 (0.5)	0	0	0
口腔カンジダ症	2 (1.0)	0	0	0
口腔真菌感染	1 (0.5)	0	0	0
細菌の過剰増殖	1 (0.5)	0	0	0
直腸周囲膿瘍	1 (0.5)	0	0	0
咽頭炎	0	1 (0.5)	1 (0.5)	2 (0.5)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
感染症および寄生虫症 (Cont.)				
細菌性咽頭炎	0	0	1 (0.5)	1 (0.2)
毛巣嚢胞	0	1 (0.5)	0	1 (0.2)
歯髄炎	0	0	1 (0.5)	1 (0.2)
鼻炎	1 (0.5)	0	0	0
敗血症	1 (0.5)	0	1 (0.5)	1 (0.2)
赤痢菌感染	1 (0.5)	0	0	0
副鼻腔炎	4 (1.9)	2 (1.0)	2 (1.0)	4 (1.0)
白癬感染	1 (0.5)	0	0	0
歯膿瘍	2 (1.0)	0	3 (1.5)	3 (0.7)
気管炎	1 (0.5)	0	0	0
上気道感染	4 (1.9)	3 (1.5)	4 (2.0)	7 (1.7)
尿路感染	3 (1.4)	4 (1.9)	1 (0.5)	5 (1.2)
ウイルス性心筋炎	1 (0.5)	0	0	0
ウイルス性咽頭炎	0	1 (0.5)	0	1 (0.2)
ウイルス性上気道感染	0	1 (0.5)	2 (1.0)	3 (0.7)
外陰部腟カンジダ症	1 (0.5)	2 (1.0)	1 (0.5)	3 (0.7)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
感染症および寄生虫症 (Cont.)				
外陰膣真菌感染	1 (0.5)	0	1 (0.5)	1 (0.2)
傷害、中毒および処置合併症	6 (2.9)	9 (4.4)	6 (2.9)	15 (3.6)
挫傷	1 (0.5)	2 (1.0)	2 (1.0)	4 (1.0)
手骨折	0	1 (0.5)	0	1 (0.2)
瘢痕ヘルニア	1 (0.5)	0	0	0
注入に伴う反応	1 (0.5)	1 (0.5)	0	1 (0.2)
四肢損傷	0	1 (0.5)	1 (0.5)	2 (0.5)
下肢骨折	1 (0.5)	0	0	0
筋断裂	0	2 (1.0)	0	2 (0.5)
肉離れ	0	1 (0.5)	0	1 (0.2)
処置後瘻孔	0	1 (0.5)	0	1 (0.2)
処置による悪心	0	0	1 (0.5)	1 (0.2)
処置による疼痛	1 (0.5)	0	0	0
交通事故	0	0	1 (0.5)	1 (0.2)
皮膚擦過傷	0	0	1 (0.5)	1 (0.2)
熱傷	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
傷害、中毒および処置合併症 (Cont.)				
各種物質毒性	1 (0.5)	0	1 (0.5)	1 (0.2)
臨床検査	11 (5.3)	9 (4.4)	4 (2.0)	13 (3.2)
細菌検査陽性	1 (0.5)	0	0	0
好塩基球数増加	0	1 (0.5)	0	1 (0.2)
血中アルブミン減少	0	1 (0.5)	0	1 (0.2)
血中ビリルビン増加	0	1 (0.5)	0	1 (0.2)
血中ブドウ糖増加	1 (0.5)	2 (1.0)	1 (0.5)	3 (0.7)
血中リン減少	0	1 (0.5)	0	1 (0.2)
クロストリジウム検査陽性	1 (0.5)	0	0	0
コクサッキーウイルス検査陽性	1 (0.5)	0	0	0
γ−グルタミルトランスフェラーゼ増加	0	0	1 (0.5)	1 (0.2)
肝酵素異常	1 (0.5)	0	0	0
肝酵素上昇	0	0	1 (0.5)	1 (0.2)
肝機能検査異常	1 (0.5)	0	0	0
リンパ球数減少	1 (0.5)	0	0	0
単球数減少	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
臨床検査 (Cont.)				
単球数増加	0	1 (0.5)	0	1 (0.2)
好中球数増加	1 (0.5)	0	0	0
総蛋白減少	1 (0.5)	0	0	0
尿中蛋白陽性	0	0	1 (0.5)	1 (0.2)
体重減少	3 (1.4)	2 (1.0)	0	2 (0.5)
体重増加	0	2 (1.0)	0	2 (0.5)
代謝および栄養障害	12 (5.8)	9 (4.4)	10 (4.9)	19 (4.6)
悪液質	1 (0.5)	0	0	0
食欲減退	3 (1.4)	2 (1.0)	0	2 (0.5)
脱水	3 (1.4)	0	0	0
痛風	1 (0.5)	0	0	0
高血糖	0	1 (0.5)	0	1 (0.2)
高トリグリセリド血症	0	2 (1.0)	2 (1.0)	4 (1.0)
低血糖	0	0	1 (0.5)	1 (0.2)
低カリウム血症	1 (0.5)	1 (0.5)	1 (0.5)	2 (0.5)
代謝低下症	0	1 (0.5)	0	1 (0.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
代謝および栄養障害 (Cont.)				
低リン酸血症	0	2 (1.0)	0	2 (0.5)
鉄欠乏	2 (1.0)	2 (1.0)	3 (1.5)	5 (1.2)
栄養障害	2 (1.0)	0	1 (0.5)	1 (0.2)
ビタミンB12欠乏	0	0	1 (0.5)	1 (0.2)
ビタミンD欠乏	0	0	1 (0.5)	1 (0.2)
筋骨格系および結合組織障害	31 (15.0)	17 (8.3)	21 (10.2)	38 (9.2)
強直性脊椎炎	1 (0.5)	1 (0.5)	0	1 (0.2)
関節痛	9 (4.3)	8 (3.9)	9 (4.4)	17 (4.1)
関節炎	2 (1.0)	0	0	0
関節障害	5 (2.4)	3 (1.5)	3 (1.5)	6 (1.5)
背部痛	5 (2.4)	0	2 (1.0)	2 (0.5)
滑液包炎	0	0	1 (0.5)	1 (0.2)
肋軟骨炎	0	1 (0.5)	0	1 (0.2)
瘻孔分泌物	0	2 (1.0)	0	2 (0.5)
側腹部痛	0	1 (0.5)	0	1 (0.2)
椎間板突出	0	1 (0.5)	0	1 (0.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
筋骨格系および結合組織障害 (Cont.)				
関節滲出液	1 (0.5)	0	0	0
関節腫脹	1 (0.5)	0	0	0
筋痙縮	0	0	1 (0.5)	1 (0.2)
筋肉痛	3 (1.4)	0	1 (0.5)	1 (0.2)
筋炎	1 (0.5)	0	0	0
頚部痛	1 (0.5)	0	0	0
骨減少症	1 (0.5)	0	0	0
骨粗鬆症	0	0	1 (0.5)	1 (0.2)
四肢痛	1 (0.5)	0	2 (1.0)	2 (0.5)
仙腸骨炎	1 (0.5)	0	0	0
変形性脊椎症	1 (0.5)	0	0	0
脊椎痛	1 (0.5)	0	0	0
脊椎関節障害	1 (0.5)	2 (1.0)	1 (0.5)	3 (0.7)
腱性拘縮	0	1 (0.5)	0	1 (0.2)
腱炎	1 (0.5)	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (1.0)	2 (1.0)	3 (1.5)	5 (1.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)				
乳房の良性新生物	1 (0.5)	0	0	0
脂漏性角化症	0	0	1 (0.5)	1 (0.2)
皮膚乳頭腫	0	2 (1.0)	0	2 (0.5)
肺扁平上皮癌	0	0	1 (0.5)	1 (0.2)
潰瘍性血管腫	1 (0.5)	0	0	0
外陰膣部疣贅	0	0	1 (0.5)	1 (0.2)
神経系障害	18 (8.7)	18 (8.7)	17 (8.3)	35 (8.5)
味覚消失	1 (0.5)	0	0	0
灼熱感	1 (0.5)	0	0	0
浮動性めまい	5 (2.4)	2 (1.0)	2 (1.0)	4 (1.0)
てんかん	0	0	1 (0.5)	1 (0.2)
頭痛	11 (5.3)	11 (5.3)	10 (4.9)	21 (5.1)
感覚鈍麻	0	2 (1.0)	0	2 (0.5)
嗜眠	2 (1.0)	0	1 (0.5)	1 (0.2)
片頭痛	0	0	2 (1.0)	2 (0.5)
錯感覚	2 (1.0)	3 (1.5)	2 (1.0)	5 (1.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
神経系障害 (Cont.)				
失神寸前の状態	0	1 (0.5)	0	1 (0.2)
下肢静止不能症候群	1 (0.5)	0	0	0
傾眠	0	1 (0.5)	0	1 (0.2)
失神	0	1 (0.5)	0	1 (0.2)
緊張性頭痛	0	1 (0.5)	0	1 (0.2)
振戦	0	1 (0.5)	0	1 (0.2)
製品の問題	1 (0.5)	0	0	0
医療機器位置異常	1 (0.5)	0	0	0
精神障害	11 (5.3)	8 (3.9)	4 (2.0)	12 (2.9)
激越	0	0	1 (0.5)	1 (0.2)
不安	3 (1.4)	1 (0.5)	2 (1.0)	3 (0.7)
燃え尽き症候群	0	1 (0.5)	0	1 (0.2)
抑うつ気分	1 (0.5)	0	0	0
うつ病	2 (1.0)	1 (0.5)	0	1 (0.2)
不眠症	6 (2.9)	3 (1.5)	1 (0.5)	4 (1.0)
睡眠障害	0	2 (1.0)	0	2 (0.5)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
腎および尿路障害	4 (1.9)	0	5 (2.4)	5 (1.2)
急性腎障害	1 (0.5)	0	0	0
尿路結石	1 (0.5)	0	0	0
慢性腎臓病	0	0	1 (0.5)	1 (0.2)
排尿困難	0	0	2 (1.0)	2 (0.5)
血尿	0	0	1 (0.5)	1 (0.2)
腎結石症	2 (1.0)	0	1 (0.5)	1 (0.2)
生殖系および乳房障害	5 (2.4)	1 (0.5)	3 (1.5)	4 (1.0)
乳房不快感	0	0	1 (0.5)	1 (0.2)
性交困難	0	1 (0.5)	0	1 (0.2)
過少月経	1 (0.5)	0	0	0
月経過多	1 (0.5)	0	1 (0.5)	1 (0.2)
不規則月経	1 (0.5)	0	0	0
卵巣静脈血栓症	0	0	1 (0.5)	1 (0.2)
会陰瘙	1 (0.5)	0	0	0
外陰腟そう痒症	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
呼吸器、胸郭および縦隔障害	14 (6.8)	6 (2.9)	9 (4.4)	15 (3.6)
急性呼吸不全	0	0	1 (0.5)	1 (0.2)
アレルギー性気管支炎	1 (0.5)	0	0	0
無気肺	0	0	1 (0.5)	1 (0.2)
気管支痙攣	0	1 (0.5)	0	1 (0.2)
慢性閉塞性肺疾患	0	0	1 (0.5)	1 (0.2)
咳嗽	6 (2.9)	1 (0.5)	0	1 (0.2)
呼吸困難	1 (0.5)	1 (0.5)	1 (0.5)	2 (0.5)
鼻出血	1 (0.5)	1 (0.5)	0	1 (0.2)
鼻閉	1 (0.5)	0	1 (0.5)	1 (0.2)
口腔咽頭痛	1 (0.5)	1 (0.5)	1 (0.5)	2 (0.5)
副鼻腔不快感	1 (0.5)	0	0	0
湿性咳嗽	1 (0.5)	0	0	0
肺塞栓症	0	0	1 (0.5)	1 (0.2)
アレルギー性鼻炎	0	0	1 (0.5)	1 (0.2)
鼻漏	2 (1.0)	0	2 (1.0)	2 (0.5)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
副鼻腔うっ血	0	1 (0.5)	0	1 (0.2)
副鼻腔痛	1 (0.5)	0	0	0
頻呼吸	1 (0.5)	0	0	0
皮膚および皮下組織障害	26 (12.6)	18 (8.7)	24 (11.7)	42 (10.2)
ざ瘡	3 (1.4)	0	2 (1.0)	2 (0.5)
脱毛症	3 (1.4)	0	3 (1.5)	3 (0.7)
皮膚炎	1 (0.5)	2 (1.0)	0	2 (0.5)
アレルギー性皮膚炎	0	0	1 (0.5)	1 (0.2)
皮膚乾燥	0	3 (1.5)	0	3 (0.7)
斑状出血	0	1 (0.5)	0	1 (0.2)
湿疹	1 (0.5)	1 (0.5)	1 (0.5)	2 (0.5)
紅斑	1 (0.5)	0	3 (1.5)	3 (0.7)
結節性紅斑	1 (0.5)	0	2 (1.0)	2 (0.5)
皮下出血	0	1 (0.5)	0	1 (0.2)
汗腺炎	0	0	1 (0.5)	1 (0.2)
多汗症	0	1 (0.5)	0	1 (0.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
皮膚および皮下組織障害 (Cont.)				
内方発育毛	0	1 (0.5)	0	1 (0.2)
寝汗	4 (1.9)	0	0	0
丘疹	0	1 (0.5)	0	1 (0.2)
光線過敏性反応	0	0	1 (0.5)	1 (0.2)
ばら色粃糠疹	1 (0.5)	0	0	0
そう痒症	4 (1.9)	2 (1.0)	0	2 (0.5)
乾癬	1 (0.5)	2 (1.0)	0	2 (0.5)
発疹	3 (1.4)	2 (1.0)	4 (2.0)	6 (1.5)
丘疹性皮疹	0	0	1 (0.5)	1 (0.2)
そう痒性皮疹	1 (0.5)	0	0	0
小水疱性皮疹	0	0	1 (0.5)	1 (0.2)
酒さ	2 (1.0)	0	0	0
皮膚変色	0	1 (0.5)	0	1 (0.2)
皮膚剥脱	1 (0.5)	1 (0.5)	0	1 (0.2)
皮膚病変	1 (0.5)	0	1 (0.5)	1 (0.2)
日光黒子	0	0	1 (0.5)	1 (0.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.1.2.3

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
皮膚および皮下組織障害 (Cont.)				
蕁麻疹	1 (0.5)	1 (0.5)	2 (1.0)	3 (0.7)
乾皮症	0	0	1 (0.5)	1 (0.2)
外科および内科処置	0	0	2 (1.0)	2 (0.5)
瘢痕ヘルニア修復	0	0	1 (0.5)	1 (0.2)
智歯抜歯	0	0	1 (0.5)	1 (0.2)
血管障害	5 (2.4)	3 (1.5)	6 (2.9)	9 (2.2)
潮紅	2 (1.0)	1 (0.5)	0	1 (0.2)
ほてり	1 (0.5)	0	1 (0.5)	1 (0.2)
高血圧	0	1 (0.5)	2 (1.0)	3 (0.7)
低血圧	0	1 (0.5)	1 (0.5)	2 (0.5)
ルリッシュ症候群	0	0	1 (0.5)	1 (0.2)
末梢血管障害	1 (0.5)	0	0	0
末梢静脈疾患	0	0	1 (0.5)	1 (0.2)
血栓性静脈炎	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表6

[redacted]20[redacted] 14:14 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
Any adverse event	19 (46.3)	20 (47.6)	24 (57.1)	43 (50.0)	106 (50.2)
血液およびリンパ系障害	0	0	0	5 (5.8)	5 (2.4)
貧血	0	0	0	3 (3.5)	3 (1.4)
リンパ球減少症	0	0	0	2 (2.3)	2 (0.9)
心臓障害	0	0	0	2 (2.3)	2 (0.9)
洞性頻脈	0	0	0	1 (1.2)	1 (0.5)
頻脈	0	0	0	1 (1.2)	1 (0.5)
内分泌障害	1 (2.4)	0	0	1 (1.2)	2 (0.9)
バセドウ病	1 (2.4)	0	0	0	1 (0.5)
クッシング症候群	0	0	0	1 (1.2)	1 (0.5)
眼障害	1 (2.4)	0	1 (2.4)	0	2 (0.9)
眼刺激	0	0	1 (2.4)	0	1 (0.5)
眼球浮腫	1 (2.4)	0	0	0	1 (0.5)
胃腸障害	7 (17.1)	7 (16.7)	12 (28.6)	16 (18.6)	42 (19.9)
腹痛	3 (7.3)	1 (2.4)	2 (4.8)	3 (3.5)	9 (4.3)
下腹部痛	0	0	1 (2.4)	0	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
胃腸障害 (Cont.)					
裂肛	0	0	0	1 (1.2)	1 (0.5)
痔瘻	0	0	1 (2.4)	0	1 (0.5)
肛門狭窄	0	0	0	1 (1.2)	1 (0.5)
口角口唇炎	0	0	0	1 (1.2)	1 (0.5)
アフタ性潰瘍	0	1 (2.4)	0	0	1 (0.5)
便秘	0	0	0	1 (1.2)	1 (0.5)
クローン病	1 (2.4)	0	4 (9.5)	5 (5.8)	10 (4.7)
下痢	1 (2.4)	1 (2.4)	0	0	2 (0.9)
鼓腸	2 (4.9)	0	0	0	2 (0.9)
胃食道逆流性疾患	0	1 (2.4)	1 (2.4)	0	2 (0.9)
吐血	0	0	0	1 (1.2)	1 (0.5)
血便排泄	0	1 (2.4)	0	0	1 (0.5)
回腸狭窄	0	0	0	1 (1.2)	1 (0.5)
腸閉塞	0	1 (2.4)	0	0	1 (0.5)
空腸狭窄	0	0	0	1 (1.2)	1 (0.5)
吸収不良	1 (2.4)	0	0	0	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
胃腸障害 (Cont.)					
悪心	1 (2.4)	1 (2.4)	3 (7.1)	0	5 (2.4)
直腸出血	1 (2.4)	0	1 (2.4)	0	2 (0.9)
直腸ポリープ	0	0	0	1 (1.2)	1 (0.5)
歯痛	0	0	1 (2.4)	0	1 (0.5)
臍ヘルニア	0	0	0	1 (1.2)	1 (0.5)
嘔吐	2 (4.9)	2 (4.8)	1 (2.4)	0	5 (2.4)
一般・全身障害および投与部位の状態	6 (14.6)	5 (11.9)	3 (7.1)	3 (3.5)	17 (8.1)
投与部位疼痛	1 (2.4)	0	0	0	1 (0.5)
無力症	1 (2.4)	1 (2.4)	0	1 (1.2)	3 (1.4)
悪寒	0	0	1 (2.4)	0	1 (0.5)
疲労	1 (2.4)	0	1 (2.4)	0	2 (0.9)
高体温症	1 (2.4)	0	0	0	1 (0.5)
硬結	1 (2.4)	0	0	0	1 (0.5)
インフルエンザ様疾患	0	1 (2.4)	0	0	1 (0.5)
注射部位紅斑	1 (2.4)	1 (2.4)	0	0	2 (0.9)
注射部位疼痛	0	0	0	1 (1.2)	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
注射部位発疹	0	1 (2.4)	0	0	1 (0.5)
疼痛	0	1 (2.4)	0	0	1 (0.5)
発熱	3 (7.3)	2 (4.8)	2 (4.8)	2 (2.3)	9 (4.3)
肝胆道系障害	1 (2.4)	0	0	0	1 (0.5)
肝障害	1 (2.4)	0	0	0	1 (0.5)
免疫系障害	0	1 (2.4)	1 (2.4)	0	2 (0.9)
過敏症	0	1 (2.4)	0	0	1 (0.5)
複合アレルギー	0	0	1 (2.4)	0	1 (0.5)
感染症および寄生虫症	5 (12.2)	7 (16.7)	7 (16.7)	20 (23.3)	39 (18.5)
肛門膿瘍	0	0	0	1 (1.2)	1 (0.5)
気管支炎	0	1 (2.4)	0	0	1 (0.5)
気管支肺アスペルギルス症	0	0	0	1 (1.2)	1 (0.5)
COVID－19	0	0	0	2 (2.3)	2 (0.9)
結膜炎	0	0	0	1 (1.2)	1 (0.5)
サイトメガロウイルス感染	0	0	0	1 (1.2)	1 (0.5)
毛包炎	0	0	0	1 (1.2)	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
感染症および寄生虫症 (Cont.)					
胃腸炎	0	0	2 (4.8)	0	2 (0.9)
単純ヘルペス	0	0	0	1 (1.2)	1 (0.5)
帯状疱疹	0	0	0	1 (1.2)	1 (0.5)
麦粒腫	0	0	0	1 (1.2)	1 (0.5)
インフルエンザ	0	0	0	1 (1.2)	1 (0.5)
爪感染	0	1 (2.4)	0	0	1 (0.5)
上咽頭炎	1 (2.4)	0	2 (4.8)	2 (2.3)	5 (2.4)
口腔カンジダ症	0	0	0	1 (1.2)	1 (0.5)
口腔ヘルペス	0	1 (2.4)	0	2 (2.3)	3 (1.4)
咽頭炎	1 (2.4)	0	0	0	1 (0.5)
肺炎	0	0	0	1 (1.2)	1 (0.5)
ブドウ球菌性肺炎	0	0	0	1 (1.2)	1 (0.5)
気道感染	0	0	0	1 (1.2)	1 (0.5)
ウイルス性気道感染	0	1 (2.4)	0	0	1 (0.5)
鼻炎	1 (2.4)	0	1 (2.4)	0	2 (0.9)
敗血症	0	0	1 (2.4)	0	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
感染症および寄生虫症 (Cont.)					
副鼻腔炎	0	1 (2.4)	1 (2.4)	0	2 (0.9)
股部白癬	0	0	0	1 (1.2)	1 (0.5)
歯膿瘍	0	1 (2.4)	0	0	1 (0.5)
上気道感染	2 (4.9)	0	1 (2.4)	2 (2.3)	5 (2.4)
尿路感染	0	0	1 (2.4)	3 (3.5)	4 (1.9)
ウイルス性上気道感染	0	1 (2.4)	0	0	1 (0.5)
外陰部炎	1 (2.4)	0	0	0	1 (0.5)
傷害、中毒および処置合併症	0	0	3 (7.1)	2 (2.3)	5 (2.4)
吻合部漏出	0	0	1 (2.4)	0	1 (0.5)
動物咬傷	0	0	0	1 (1.2)	1 (0.5)
耳介血腫	0	0	1 (2.4)	0	1 (0.5)
処置後出血	0	0	0	1 (1.2)	1 (0.5)
瘢痕	0	0	1 (2.4)	0	1 (0.5)
臨床検査	0	3 (7.1)	0	2 (2.3)	5 (2.4)
血中重炭酸塩減少	0	1 (2.4)	0	0	1 (0.5)
血中トリグリセリド増加	0	0	0	1 (1.2)	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
臨床検査 (Cont.)					
ヘモグロビン減少	0	0	0	1 (1.2)	1 (0.5)
肝酵素上昇	0	1 (2.4)	0	0	1 (0.5)
体重増加	0	1 (2.4)	0	0	1 (0.5)
代謝および栄養障害	1 (2.4)	0	1 (2.4)	1 (1.2)	3 (1.4)
糖尿病	1 (2.4)	0	0	0	1 (0.5)
低リン酸血症	0	0	0	1 (1.2)	1 (0.5)
栄養障害	0	0	1 (2.4)	0	1 (0.5)
筋骨格系および結合組織障害	5 (12.2)	2 (4.8)	6 (14.3)	7 (8.1)	20 (9.5)
関節痛	2 (4.9)	1 (2.4)	1 (2.4)	5 (5.8)	9 (4.3)
関節障害	1 (2.4)	0	0	0	1 (0.5)
背部痛	1 (2.4)	1 (2.4)	0	1 (1.2)	3 (1.4)
関節硬直	0	0	1 (2.4)	0	1 (0.5)
関節腫脹	0	0	1 (2.4)	0	1 (0.5)
筋痙縮	0	0	1 (2.4)	0	1 (0.5)
筋骨格痛	1 (2.4)	0	0	0	1 (0.5)
筋肉痛	0	0	1 (2.4)	1 (1.2)	2 (0.9)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
筋骨格系および結合組織障害 (Cont.)					
腱炎	0	0	1 (2.4)	0	1 (0.5)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む)	0	0	0	1 (1.2)	1 (0.5)
メラノサイト性母斑	0	0	0	1 (1.2)	1 (0.5)
神経系障害	1 (2.4)	1 (2.4)	5 (11.9)	5 (5.8)	12 (5.7)
頭痛	1 (2.4)	1 (2.4)	3 (7.1)	4 (4.7)	9 (4.3)
嗜眠	0	0	1 (2.4)	0	1 (0.5)
片頭痛	0	0	1 (2.4)	0	1 (0.5)
振戦	0	0	0	1 (1.2)	1 (0.5)
妊娠、産褥および周産期の状態	0	1 (2.4)	0	0	1 (0.5)
自然流産	0	1 (2.4)	0	0	1 (0.5)
精神障害	1 (2.4)	0	1 (2.4)	0	2 (0.9)
不安	0	0	1 (2.4)	0	1 (0.5)
不眠症	1 (2.4)	0	0	0	1 (0.5)
腎および尿路障害	1 (2.4)	1 (2.4)	0	1 (1.2)	3 (1.4)
急性腎障害	0	0	0	1 (1.2)	1 (0.5)
血尿	0	1 (2.4)	0	0	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
腎および尿路障害 (Cont.)					
失禁	1 (2.4)	0	0	0	1 (0.5)
呼吸器、胸郭および縦隔障害	1 (2.4)	2 (4.8)	1 (2.4)	2 (2.3)	6 (2.8)
気管支痙攣	0	1 (2.4)	0	0	1 (0.5)
発声障害	0	1 (2.4)	0	0	1 (0.5)
呼吸困難	0	0	1 (2.4)	0	1 (0.5)
鼻漏	0	0	0	1 (1.2)	1 (0.5)
咽喉刺激感	0	0	0	1 (1.2)	1 (0.5)
上気道うっ血	1 (2.4)	0	0	0	1 (0.5)
皮膚および皮下組織障害	3 (7.3)	3 (7.1)	3 (7.1)	5 (5.8)	14 (6.6)
ざ瘡	1 (2.4)	0	0	0	1 (0.5)
脱毛症	0	1 (2.4)	0	1 (1.2)	2 (0.9)
円形脱毛症	0	1 (2.4)	0	0	1 (0.5)
皮膚炎	0	1 (2.4)	0	0	1 (0.5)
湿疹	0	1 (2.4)	0	0	1 (0.5)
多汗症	0	0	0	1 (1.2)	1 (0.5)
そう痒症	1 (2.4)	0	1 (2.4)	1 (1.2)	3 (1.4)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.2.1

Subjects with Treatment-Emergent Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
皮膚および皮下組織障害 (Cont.)					
壊疽性膿皮症	1 (2.4)	0	0	0	1 (0.5)
発疹	0	0	1 (2.4)	1 (1.2)	2 (0.9)
皮膚刺激	0	0	1 (2.4)	0	1 (0.5)
皮膚病変	0	0	0	1 (1.2)	1 (0.5)
血管障害	0	1 (2.4)	2 (4.8)	2 (2.3)	5 (2.4)
ほてり	0	1 (2.4)	0	1 (1.2)	2 (0.9)
高血圧	0	0	1 (2.4)	1 (1.2)	2 (0.9)
表在性血栓性静脈炎	0	0	1 (2.4)	0	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表7

[redacted]20[redacted] 14:14 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.1.3.5

Subjects with Treatment-Emergent Adverse Events Leading to Death by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
Any adverse event	0	0	1 (0.5)	1 (0.2)
呼吸器、胸郭および縦隔障害	0	0	1 (0.5)	1 (0.2)
急性呼吸不全	0	0	1 (0.5)	1 (0.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表8

[redacted]20[redacted] 14:14 <[redacted]>
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.2.3.3

Subjects with Treatment-Emergent Adverse Events Leading to Death by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
Any adverse event	0	0	1 (2.4)	0	1 (0.5)
感染症および寄生虫症	0	0	1 (2.4)	0	1 (0.5)
敗血症	0	0	1 (2.4)	0	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表9

[redacted]20[redacted] 14:14 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL

TABLE 14.3__2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
Any adverse event	26 (12.6)	10 (4.9)	9 (4.4)	19 (4.6)
血液およびリンパ系障害	1 (0.5)	2 (1.0)	2 (1.0)	4 (1.0)
貧血	0	2 (1.0)	2 (1.0)	4 (1.0)
骨髄機能不全	1 (0.5)	0	0	0
骨髄抑制	1 (0.5)	0	0	0
心臓障害	0	1 (0.5)	0	1 (0.2)
心房粗動	0	1 (0.5)	0	1 (0.2)
胃腸障害	23 (11.1)	4 (1.9)	1 (0.5)	5 (1.2)
腹痛	1 (0.5)	0	0	0
痔瘻	0	1 (0.5)	0	1 (0.2)
肛門括約筋無緊張症	1 (0.5)	0	0	0
肛門直腸障害	1 (0.5)	0	0	0
クローン病	20 (9.7)	1 (0.5)	1 (0.5)	2 (0.5)
細菌叢異常	1 (0.5)	0	0	0
血便排泄	0	1 (0.5)	0	1 (0.2)
回腸狭窄	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
胃腸障害 (Cont.)				
イレウス	0	1 (0.5)	0	1 (0.2)
麻痺性イレウス	1 (0.5)	0	0	0
悪心	1 (0.5)	0	0	0
小腸閉塞	2 (1.0)	1 (0.5)	0	1 (0.2)
一般・全身障害および投与部位の状態	1 (0.5)	0	1 (0.5)	1 (0.2)
発熱	1 (0.5)	0	1 (0.5)	1 (0.2)
肝胆道系障害	0	1 (0.5)	0	1 (0.2)
胆管狭窄	0	1 (0.5)	0	1 (0.2)
感染症および寄生虫症	5 (2.4)	1 (0.5)	2 (1.0)	3 (0.7)
腹部膿瘍	1 (0.5)	0	0	0
男性外性器蜂巣炎	1 (0.5)	0	0	0
大腸菌性胃腸炎	0	0	1 (0.5)	1 (0.2)
好中球減少性敗血症	1 (0.5)	0	0	0
直腸周囲膿瘍	1 (0.5)	0	0	0
敗血症	1 (0.5)	0	1 (0.5)	1 (0.2)
ウイルス性心筋炎	1 (0.5)	0	0	0

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
感染症および寄生虫症 (Cont.)				
ウイルス性咽頭炎	0	1 (0.5)	0	1 (0.2)
代謝および栄養障害	1 (0.5)	0	0	0
悪液質	1 (0.5)	0	0	0
筋骨格系および結合組織障害	1 (0.5)	1 (0.5)	0	1 (0.2)
関節痛	1 (0.5)	0	0	0
椎間板突出	0	1 (0.5)	0	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	1 (0.5)	1 (0.2)
肺扁平上皮癌	0	0	1 (0.5)	1 (0.2)
腎および尿路障害	2 (1.0)	0	1 (0.5)	1 (0.2)
急性腎障害	1 (0.5)	0	0	0
尿路結石	1 (0.5)	0	0	0
腎結石症	0	0	1 (0.5)	1 (0.2)
呼吸器、胸郭および縦隔障害	0	0	2 (1.0)	2 (0.5)
急性呼吸不全	0	0	1 (0.5)	1 (0.2)
肺塞栓症	0	0	1 (0.5)	1 (0.2)
外科および内科処置	0	0	1 (0.5)	1 (0.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class
and Preferred Term during the 12-Week Induction Period
(SA1 Population)

System Organ Class MedDRA 23.1 Preferred Term	Placebo IV (N=207) n (%)	Risankizumab 600 mg IV (N=206) n (%)	Risankizumab 1200 mg IV (N=205) n (%)	Risankizumab Total (N=411) n (%)
外科および内科処置 (Cont.)				
瘢痕ヘルニア修復	0	0	1 (0.5)	1 (0.2)
血管障害	0	0	1 (0.5)	1 (0.2)
ルリッシュ症候群	0	0	1 (0.5)	1 (0.2)

Note: Treatment emergent AEs (TEAEs) for the 12-Week Induction Period are defined as events that begin either on or after the first dose of the study drug in the 12-Week Induction Period and until the first dose of study drug in the study M16-000 if the subject is enrolled into the study M16-000 or until first dose of study drug in Induction Period 2 if the subject is enrolled into Induction Period 2, or within 140 days after the last dose administration of the study drug in 12-Week Induction Period if the subject does not participate in the study M16-000 or the Induction Period 2.
SA1 Population includes all subjects who received at least one dose of study drug during the 12-Week Induction Period.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表10

[redacted]20[redacted] 14:14 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M15-991
R&D/20/0587 - CLINICAL/STATISTICAL

TABLE 14.3__2.2.1.1

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
Any adverse event	2 (4.9)	2 (4.8)	3 (7.1)	9 (10.5)	16 (7.6)
血液およびリンパ系障害	0	0	0	1 (1.2)	1 (0.5)
貧血	0	0	0	1 (1.2)	1 (0.5)
胃腸障害	2 (4.9)	1 (2.4)	2 (4.8)	5 (5.8)	10 (4.7)
腹痛	2 (4.9)	0	0	0	2 (0.9)
肛門狭窄	0	0	0	1 (1.2)	1 (0.5)
クローン病	0	0	2 (4.8)	2 (2.3)	4 (1.9)
回腸狭窄	0	0	0	1 (1.2)	1 (0.5)
腸閉塞	0	1 (2.4)	0	0	1 (0.5)
空腸狭窄	0	0	0	1 (1.2)	1 (0.5)
悪心	1 (2.4)	0	0	0	1 (0.5)
臍ヘルニア	0	0	0	1 (1.2)	1 (0.5)
一般・全身障害および投与部位の状態	1 (2.4)	0	0	0	1 (0.5)
発熱	1 (2.4)	0	0	0	1 (0.5)
感染症および寄生虫症	0	0	1 (2.4)	3 (3.5)	4 (1.9)
肛門膿瘍	0	0	0	1 (1.2)	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__2.2.1.1

Subjects with Treatment-Emergent Serious Adverse Events by System Organ Class
and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=41) n (%)	Risankizumab 360 mg SC (N=42) n (%)	Risankizumab 1200 mg IV (N=42) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=86) n (%)	Total (N=211) n (%)
感染症および寄生虫症 (Cont.)					
気管支肺アスペルギルス症	0	0	0	1 (1.2)	1 (0.5)
サイトメガロウイルス感染	0	0	0	1 (1.2)	1 (0.5)
ブドウ球菌性肺炎	0	0	0	1 (1.2)	1 (0.5)
敗血症	0	0	1 (2.4)	0	1 (0.5)
傷害、中毒および処置合併症	0	0	1 (2.4)	1 (1.2)	2 (0.9)
吻合部漏出	0	0	1 (2.4)	0	1 (0.5)
処置後出血	0	0	0	1 (1.2)	1 (0.5)
妊娠、産褥および周産期の状態	0	1 (2.4)	0	0	1 (0.5)
自然流産	0	1 (2.4)	0	0	1 (0.5)
腎および尿路障害	0	0	0	1 (1.2)	1 (0.5)
急性腎障害	0	0	0	1 (1.2)	1 (0.5)

Note: Treatment-emergent AEs (TEAEs) for the Induction Period 2 are defined as events that begin either on or after the first dose of the study medication in the Induction Period 2 and until first dose of study drug in the Study M16-000 if the subject is enrolled into the Study M16-000 or within 140 days after the last dose of the study drug in the Induction Period 2 if the subject does not participate in the Study M16-000.
SA2 Population includes all subjects who received at least one dose of study drug during the Induction Period 2.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

M15-9　89 試験

治験の標題： An Open Label, Single Group, Long Term Safety Extension Trial of BI 655066/ABBV-066 (Risankizumab), in Patients with Moderately to Severely Active Crohn's Disease	
施設数 / 実施国名： 28 施設 / 9 ヵ国（ベルギー，カナダ，ドイツ，オランダ，ポーランド，スペイン，韓国，イギリス，米国）	
治験責任医師： Prof. Dr. [redacted]，他	
公表文献 (参考資料) ： 3 報	
治験期間： 最初の被験者の初回来院日：2015 年 9 月 16 日 最後の被験者の最終来院日：2019 年 6 月 19 日	開発のフェーズ：II
治験の種類： 非盲検，単群，長期継続投与	
目的： 主要目的 先行試験（M15-993 試験）でリサンキズマブ投与によりクローン病活動度指数（以下「CDAI」）に基づく臨床的改善（以下「臨床的 CDAI 改善」）又は臨床的寛解（以下「臨床的 CDAI 寛解」）を示し，引き続き長期投与されている中等症から重症の活動性クローン病の被験者を対象に，リサンキズマブの長期安全性を評価する。 その他の目的 リサンキズマブの長期有効性，忍容性，薬物動態，薬力学及び免疫原性を評価する。	
被験者数 (計画時と解析時) ： 計画時：約 60 例 解析時：65 例	
診断と主要な組入れ基準： 選択基準 先行試験の M15-993 試験にて以下のいずれかに該当し，試験を完了したクローン病患者とした。 • M15-993 試験の第 2 ピリオドを完了しており，Visit E1 時に臨床的 CDAI 改善（CDAI がベースラインから 100 以上の減少）がみられるものの，臨床的 CDAI 寛解（CDAI が 150 未満）には該当しない。 • M15-993 試験の第 3 ピリオドを完了しており，Visit E5 時に臨床的 CDAI 改善（CDAI がベースラインから 100 以上の減少），及び / 又は臨床的 CDAI 寛解（CDAI が 150 未満）がみられる。 • 治験実施計画書に従って M15-993 試験の第 2 ピリオド又は第 3 ピリオドを完了しており，本試験開始前にみられた臨床的 CDAI 改善又は臨床的 CDAI 寛解が維持されている，若しくは改善又は寛解が消失した場合には非盲検下で静脈内（以下「IV」）投与による再導入療法を実施している。 除外基準 • 先行試験にて主な治験の手順（大腸内視鏡検査，治療遵守，評価項目の評価，避妊法）を遵守しなかった者 • 忍容性がない又は先行試験での安全性上の理由によりリサンキズマブの投与が忍容できない者 • 妊娠中の者，授乳中の者，又は治験参加期間中若しくは治験薬の最終投与後 20 週以内に妊娠を計画している者	

- 被験者は，試験期間中又は治験薬の最終投与後 12 ヵ月までの期間，生ワクチン又は Bacille Calmette-Guérin ワクチンを受けないことに同意することとした。
- 先行試験期間中に悪性腫瘍が発現した，又は活動性悪性腫瘍疾患の疑いがあった者
- 本試験参加期間中に，治験薬や治験治療を使用する他の臨床試験に参加する意思のある者
- 併用薬の規定に従うことができない者

治験方法：

M15-993 試験終了時又は本試験のスクリーニング時に臨床的 CDAI 改善又は臨床的 CDAI 寛解であった被験者は M15-993 試験から本試験へ移行し，リサンキズマブ 180 mg を Visit 2 から治験終了時（以下「EOT」）Visit まで 8 週間ごと（以下「Q8W」）に皮下（以下「SC」）投与された。M15-993 試験の EOT 来院時又は本試験のスクリーニング時に臨床的 CDAI 寛解が消失した被験者については，非盲検下でリサンキズマブ 600 mg を 4 週間ごと（以下「Q4W」）に 3 回 IV 投与する再導入療法を行い，その後適格性を再評価した。臨床的 CDAI 改善又は臨床的 CDAI 寛解が達成された場合，Visit 5 以降はリサンキズマブ 180 mg を Q8W で SC 投与する維持療法に切り替えた。本試験を完了した被験者は，引き続き M16-000 試験 Sub-study 3（以下「SS3」）（第 III 相非盲検継続投与試験）に移行可能とした。

被験薬，用量，投与方法及びバッチ番号：

非盲検：リサンキズマブ 180 mg を Q8W で SC 投与（維持療法），及びリサンキズマブ 600 mg を Q4W で IV 投与（再導入療法）

バッチ番号：

リサンキズマブ 90 mg 静注溶液，1 mL プレフィルドシリンジ：[redacted]

リサンキズマブ 180 mg（90 mg/mL シリンジ 2 本入り）：[redacted]，[redacted]，[redacted]，[redacted]，[redacted]

リサンキズマブ非盲検 IV 投与用 100 mg/10 mL バイアル：[redacted]

治療期間：

約 4 年間。EOT のすべての治験手順を含め，本試験を完了した被験者は，引き続き M16-000 試験 SS3 に移行可能とした。

対照薬，用量，投与方法及びバッチ番号：

該当なし

評価基準：

有効性：

主要評価項目は，臨床的 CDAI 寛解，臨床的 CDAI 改善，患者報告アウトカム-2（以下「PRO-2」）寛解，PRO-2 改善，Crohn's Disease Endoscopic Index of Severity（以下「CDEIS」）に基づく内視鏡的寛解（以下「内視鏡的 CDEIS 寛解」）又は内視鏡的改善（以下「内視鏡的 CDEIS 改善」），内視鏡的粘膜治癒，完全寛解，炎症性腸疾患質問票（以下「IBDQ」）寛解，及び IBDQ 改善などとした。

薬物動態及び免疫原性：

血漿中リサンキズマブ濃度を測定した。免疫原性を評価するため，リサンキズマブに対する抗薬物抗体及び中和抗体を測定した。

安全性：

身体検査，バイタルサイン（血圧，心拍数，口腔内体温），12 誘導心電図，臨床検査（血液学的検査，血液生化学的検査及び尿検査），有害事象

統計手法：

本非盲検継続試験では統計モデルを使用しなかったため，評価項目について記述的に要約した。

有効性の結果

有効性評価項目である臨床的 CDAI 寛解，臨床的 CDAI 改善，PRO-2 寛解，PRO-2 改善，内視鏡的 CDEIS 寛解，内視鏡的 CDEIS 改善，内視鏡的粘膜治癒，完全寛解，IBDQ 寛解及び IBDQ 改善において，大部分の被験者で長期投与時にも改善傾向が維持された（Observed case 解析）。主要な副次評価項目である臨床的 CDAI 寛解（CDAI が 150 未満）及び内視鏡的 CDEIS 寛解（CDEIS が 4 以下，又は病変が回腸に限局している被験者では CDEIS が 2 以下）は，治験参加期間をとおして維持された。本試験終了時には非盲検継続投与中の被験者を第 III 相非盲検継続試験である M16-000 試験 SS3 へ移行可能としたため，本非盲検継続試験の副次評価項目である有効性の結果は observed data を用いて示しており，本試験の結果より，有効性の結論を強く支持することを意図したものではなかった。

薬物動態及び免疫原性の結果

中等症から重症のクローン病を有する全組入れ被験者にリサンキズマブ 180 mg を Q8W で SC 投与したとき，血漿曝露量は初回の SC 投与後 24 週時までに定常状態に達し，トラフ濃度の中央値は 3.66–4.23 µg/mL の範囲であった。

全体で，試験期間中にリサンキズマブを 1 回以上投与された 65 例のうち 8 例（12%）で抗薬物抗体の発現が認められたが，おおむね抗体価は低値であり（抗体価 1–64），中和抗体は認められなかった。抗薬物抗体の発現によるリサンキズマブの血漿曝露量への明確な影響は認められなかった。

安全性の結果

本非盲検継続試験において，リサンキズマブはおおむね安全で忍容性は良好であることが示された。ほとんどの被験者（92.3%［60/65 例］）で有害事象が報告され，発現割合が高かった有害事象は上咽頭炎，胃腸炎，疲労，腹痛，クローン病，関節痛及び悪心であった。重症度は多くが軽度又は中等度で，リサンキズマブの投与中止に至った有害事象はごく少数であった。発現割合が高かった重篤な有害事象はクローン病，腸管狭窄，ウイルス性胃腸炎，腹膜炎及び処置後合併症であった。2 例以上で報告された重篤な有害事象は消化管に関するものであり，基礎疾患のクローン病が影響している可能性がある。特に注目すべき事象については，悪性腫瘍又は心血管イベントと判定された事象は報告されなかった。治験薬投与後に真菌感染及び日和見感染症，過敏症の事象及び肝関連事象が数例の被験者で認められた。結核又は帯状疱疹は報告されなかった。フェインジェクト®静注に対するアナフィラキシー反応の重篤な有害事象が 1 件発現し，治験責任（分担）医師は中等度でリサンキズマブと関連なしと評価した。当該被験者はリサンキズマブの投与を継続した。試験期間中に死亡は報告されなかった。臨床検査値，バイタルサイン及び心電図に臨床的に意義のある変化は認められなかった。

結論

本試験は単群，非盲検継続投与試験であり，中等症から重症の活動性クローン病患者を対象としてリサンキズマブの長期安全性及び有効性を評価した。本試験では，維持療法としてリサンキズマブ 180 mg を Q8W で SC 投与した。M15-993 試験完了時から本試験組入れまでの間に改善又は寛解が消失した被験者は，リサンキズマブ 600 mg を Q4W で 3 回 IV 投与する再導入療法を実施後，維持療法としてリサンキズマブ 180 mg を Q8W で SC 投与した。組み入れられた 65 例のうち 44 例が試験を完了し，第 III 相試験の M16-000 試験 SS3 に移行した。主な中止理由は有害事象，同意撤回及びその他の理由であった。発現割合が高かった有害事象は上咽頭炎，胃腸炎，疲労，腹痛，クローン病，関節痛及び悪心であった。ほとんどの有害事象は軽度又は中等度で，リサンキズマブの投与中止に至った有害事象はごく少数であった。発現割合が高かった重篤な有害事象はクローン病，腸管狭窄，ウイルス性胃腸炎，腹膜炎及び処置後合併症であった。重篤な有害事象のほとんどは消化管に関連するものであり，基礎疾患のクローン病が影響している可能性がある。特に注目すべき事象については，悪性腫瘍又は心血管イベントと判定された事象は認められなかった。投与後に発現した感染症，過敏症の事象及び肝関連事象はほとんど認められず，おおむね軽度又は中等度であった。死亡は認められなかった。本試験では，リサンキズマブは安全で忍容性は良好であり，安全性に関する新たなシグナルは特定されなかった。

本試験の曝露状況の概要及び本試験で発現した有害事象を以下のとおり示す。

項目	表番号
曝露状況の概要	表 1
有害事象の概要	表 2
すべての有害事象	表 3
重篤な有害事象	表 4

表1

[redacted]20[redacted] 11:08 <[redacted]>
RISANKIZUMAB (CROHN'S)
M15-989 ABBREVIATED CLINICAL STUDY REPORT
R&D/19/0019 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.1 7
EXTENT OF EXPOSURE
(SAFETY ANALYSIS SET)

	RISANKIZUMAB 600 MG IV Q4W (N=4)	RISANKIZUMAB 180 MG SC Q8W (N=65)	ALL RISANKIZUMAB (N=65)
DURATION (DAY)			
n	4	65	65
MEAN (SD)	84.0 (1.63)	903.6 (344.39)	909.0 (343.51)
MEDIAN	84.0	1014.0	1014.0
MIN, MAX	82, 86	114, 1302	114, 1317
DURATION INTERVAL (DAY) - n (%)			
1 - 84	3 (75.0)	0	0
85 - 140	1 (25.0)	1 (1.5)	1 (1.5)
141 - 196	0	3 (4.6)	2 (3.1)
197 - 252	0	2 (3.1)	3 (4.6)
253 - 308	0	0	0
309 - 364	0	3 (4.6)	3 (4.6)
365 - 420	0	1 (1.5)	1 (1.5)
421 - 476	0	1 (1.5)	1 (1.5)
477 - 532	0	1 (1.5)	1 (1.5)
533 - 588	0	1 (1.5)	1 (1.5)
589 - 644	0	1 (1.5)	1 (1.5)
645 - 700	0	1 (1.5)	0
701 - 756	0	2 (3.1)	3 (4.6)
757 - 812	0	1 (1.5)	1 (1.5)
813 - 868	0	1 (1.5)	1 (1.5)
869 - 924	0	6 (9.2)	6 (9.2)
>924	0	40 (61.5)	40 (61.5)
MISSING	0	0	0

NOTE: FOR RISANKIZUMAB 600 MG IV Q4W: DURATION = MIN (FIRST SC DOSE DATE IN OPEN LABEL MAINTENANCE PERIOD - FIRST IV DOSE DATE IN OPEN LABEL RE-INDUCTION PERIOD, LAST IV DOSE DATE IN OPEN LABEL RE-INDUCTION PERIOD - FIRST IV DOSE DATE IN OPEN LABEL RE-INDUCTION PERIOD + 28). FOR RISANKIZUMAB 180 MG SC Q8W: DURATION = MIN (LAST SC DOSE DATE IN OPEN LABEL MAINTENANCE PERIOD - FIRST SC DOSE DATE IN OPEN LABEL MAINTENANCE PERIOD + 56, FIRST DOSE DATE OF STUDY DRUG IN M16-000 SUB-STUDY 3 - FIRST SC DOSE DATE IN OPEN LABEL MAINTENANCE PERIOD). FOR ALL RISANKIZUMAB: DURATION = MIN (LAST DOSE DATE OF STUDY DRUG IN M15-989 - FIRST DOSE DATE OF STUDY DRUG IN M15-989 + 56, FIRST DOSE DATE OF STUDY DRUG IN M16-000 SUB-STUDY 3 - FIRST DOSE DATE OF STUDY DRUG IN M15-989).

Program Source Code: [redacted]

表2

[redacted]20[redacted] 01:32 <[redacted]>
RISANKIZUMAB (CROHN'S)
M15-989 ABBREVIATED CLINICAL STUDY REPORT
R&D/19/0019 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__1.1.1

Overview of Treatment-Emergent Adverse Events and All Deaths
(Safety Analysis Set)

	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
Subjects with any treatment-emergent			
Adverse event (AE)	2 (50.0)	60 (92.3)	60 (92.3)
AE with reasonable possibility of being drug related$	1 (25.0)	26 (40.0)	26 (40.0)
Severe AE+	0	14 (21.5)	14 (21.5)
Serious AE	0	23 (35.4)	23 (35.4)
AE leading to discontinuation of study drug	0	6 (9.2)	6 (9.2)
AE leading to death	0	0	0
Serious infections	0	6 (9.2)	6 (9.2)
Tuberculosis	0	0	0
Opportunistic infections	0	3 (4.6)	3 (4.6)
Malignant tumours	0	0	0
Malignancies excluding NMSC	0	0	0
Hypersensitivity	0	16 (24.6)	16 (24.6)
Anaphylactic reaction	0	1 (1.5)	1 (1.5)
Adjudicated MACE	0	0	0
All deaths	0	0	0
Occurring <= 140 days after last dose	0	0	0
Occurring > 140 days after last dose	0	0	0

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3.
Subjects are counted once in each row, regardless of the number of events they may have had.
Adverse events with unknown relationship were counted as 'REASONABLE POSSIBILITY RELATED'.
$ As assessed by investigator.
+ NCI toxicity grade of 3 and above is considered as severe. Adverse events with unknown toxicity were counted as 'SEVERE'.

Program Source Code: [redacted]

表3

[redacted]20[redacted] 01:32 <[redacted] >
RISANKIZUMAB (CROHN'S)
M15-989 ABBREVIATED CLINICAL STUDY REPORT
R&D/19/0019 - CLINICAL/STATISTICAL

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
Any adverse event	2 (50.0)	60 (92.3)	60 (92.3)
血液およびリンパ系障害	0	6 (9.2)	6 (9.2)
貧血	0	2 (3.1)	2 (3.1)
内出血発生の増加傾向	0	1 (1.5)	1 (1.5)
鉄欠乏性貧血	0	1 (1.5)	1 (1.5)
白血球減少症	0	2 (3.1)	2 (3.1)
好中球減少症	0	2 (3.1)	2 (3.1)
血小板増加症	0	1 (1.5)	1 (1.5)
心臓障害	0	4 (6.2)	4 (6.2)
狭心症	0	1 (1.5)	1 (1.5)
期外収縮	0	1 (1.5)	1 (1.5)
動悸	0	2 (3.1)	2 (3.1)
頻脈	0	2 (3.1)	2 (3.1)
耳および迷路障害	1 (25.0)	2 (3.1)	3 (4.6)
耳痛	1 (25.0)	0	1 (1.5)
回転性めまい	0	2 (3.1)	2 (3.1)
内分泌障害	0	2 (3.1)	2 (3.1)
副腎機能不全	0	1 (1.5)	1 (1.5)
甲状腺機能低下症	0	1 (1.5)	1 (1.5)
眼障害	0	2 (3.1)	2 (3.1)
結膜充血	0	1 (1.5)	1 (1.5)
眼の異物感	0	1 (1.5)	1 (1.5)
硝子体剥離	0	1 (1.5)	1 (1.5)
胃腸障害	2 (50.0)	44 (67.7)	45 (69.2)
腹部不快感	0	1 (1.5)	1 (1.5)
腹部膨満	0	4 (6.2)	4 (6.2)
腹痛	0	12 (18.5)	12 (18.5)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
胃腸障害 (Cont.)	2 (50.0)	44 (67.7)	45 (69.2)
下腹部痛	0	1 (1.5)	1 (1.5)
上腹部痛	1 (25.0)	5 (7.7)	6 (9.2)
腹部圧痛	0	1 (1.5)	1 (1.5)
裂肛	0	2 (3.1)	2 (3.1)
痔瘻	0	2 (3.1)	2 (3.1)
肛門失禁	0	1 (1.5)	1 (1.5)
肛門ポリープ	0	1 (1.5)	1 (1.5)
肛門そう痒症	0	1 (1.5)	1 (1.5)
肛門狭窄	0	1 (1.5)	1 (1.5)
肛門潰瘍	0	1 (1.5)	1 (1.5)
アフタ性潰瘍	0	2 (3.1)	2 (3.1)
便秘	0	4 (6.2)	4 (6.2)
クローン病	0	12 (18.5)	12 (18.5)
下痢	0	8 (12.3)	8 (12.3)
ダンピング症候群	0	1 (1.5)	1 (1.5)
消化不良	0	2 (3.1)	2 (3.1)
小腸炎	0	2 (3.1)	2 (3.1)
糞塊	0	1 (1.5)	1 (1.5)
変色便	0	1 (1.5)	1 (1.5)
鼓腸	0	1 (1.5)	1 (1.5)
食中毒	0	1 (1.5)	1 (1.5)
排便回数増加	0	1 (1.5)	1 (1.5)
胃食道逆流性疾患	0	4 (6.2)	4 (6.2)
舌炎	0	1 (1.5)	1 (1.5)
血便排泄	1 (25.0)	2 (3.1)	2 (3.1)
痔核	0	2 (3.1)	2 (3.1)
回腸狭窄	0	2 (3.1)	2 (3.1)
イレウス	0	1 (1.5)	1 (1.5)
胃排出不全	0	1 (1.5)	1 (1.5)
鼠径ヘルニア	0	1 (1.5)	1 (1.5)
腸閉塞	0	1 (1.5)	1 (1.5)
腸管狭窄	0	2 (3.1)	2 (3.1)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
胃腸障害 (Cont.)	2 (50.0)	44 (67.7)	45 (69.2)
過敏性腸症候群	0	1 (1.5)	1 (1.5)
弛緩歯	0	1 (1.5)	1 (1.5)
口腔内潰瘍形成	0	2 (3.1)	2 (3.1)
悪心	0	10 (15.4)	10 (15.4)
嚥下痛	1 (25.0)	0	1 (1.5)
肛門周囲痛	0	2 (3.1)	2 (3.1)
偽性ポリポーシス	0	1 (1.5)	1 (1.5)
小腸閉塞	0	1 (1.5)	1 (1.5)
小腸ポリープ	0	1 (1.5)	1 (1.5)
口内炎	0	1 (1.5)	1 (1.5)
歯の障害	0	1 (1.5)	1 (1.5)
歯痛	0	2 (3.1)	2 (3.1)
臍ヘルニア	0	1 (1.5)	1 (1.5)
嘔吐	1 (25.0)	4 (6.2)	5 (7.7)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
一般・全身障害および投与部位の状態	0	26 (40.0)	26 (40.0)
無力症	0	3 (4.6)	3 (4.6)
腋窩痛	0	1 (1.5)	1 (1.5)
胸痛	0	2 (3.1)	2 (3.1)
嚢胞	0	1 (1.5)	1 (1.5)
不快感	0	1 (1.5)	1 (1.5)
顔面浮腫	0	1 (1.5)	1 (1.5)
疲労	0	13 (20.0)	13 (20.0)
インフルエンザ様疾患	0	2 (3.1)	2 (3.1)
注射部位紅斑	0	3 (4.6)	3 (4.6)
注射部位過敏反応	0	1 (1.5)	1 (1.5)
注射部位疼痛	0	3 (4.6)	3 (4.6)
注射部位そう痒感	0	1 (1.5)	1 (1.5)
注射部位反応	0	1 (1.5)	1 (1.5)
注射部位腫脹	0	1 (1.5)	1 (1.5)
医療機器関連損傷	0	1 (1.5)	1 (1.5)
末梢性浮腫	0	1 (1.5)	1 (1.5)
疼痛	0	2 (3.1)	2 (3.1)
末梢腫脹	0	2 (3.1)	2 (3.1)
発熱	0	2 (3.1)	2 (3.1)
恥骨上痛	0	1 (1.5)	1 (1.5)
肝胆道系障害	0	3 (4.6)	3 (4.6)
胆嚢炎	0	1 (1.5)	1 (1.5)
肝機能異常	0	1 (1.5)	1 (1.5)
脂肪肝	0	1 (1.5)	1 (1.5)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
免疫系障害	0	4 (6.2)	4 (6.2)
アナフィラキシー反応	0	1 (1.5)	1 (1.5)
食物アレルギー	0	1 (1.5)	1 (1.5)
季節性アレルギー	0	2 (3.1)	2 (3.1)
感染症および寄生虫症	2 (50.0)	48 (73.8)	48 (73.8)
膿瘍	0	1 (1.5)	1 (1.5)
肛門膿瘍	0	2 (3.1)	2 (3.1)
ブラストシスティス感染	0	1 (1.5)	1 (1.5)
ボトリオミセス症	0	1 (1.5)	1 (1.5)
気管支炎	0	3 (4.6)	3 (4.6)
カンピロバクター感染	0	1 (1.5)	1 (1.5)
クラミジア感染	0	1 (1.5)	1 (1.5)
結膜炎	0	3 (4.6)	3 (4.6)
膀胱炎	0	3 (4.6)	3 (4.6)
耳感染	0	4 (6.2)	4 (6.2)
蟯虫症	0	1 (1.5)	1 (1.5)
丹毒	0	1 (1.5)	1 (1.5)
眼感染	0	1 (1.5)	1 (1.5)
真菌感染	0	1 (1.5)	1 (1.5)
真菌性食道炎	0	1 (1.5)	1 (1.5)
皮膚真菌感染	0	1 (1.5)	1 (1.5)
胃腸炎	0	15 (23.1)	15 (23.1)
ウイルス性胃腸炎	0	4 (6.2)	4 (6.2)
消化管感染	0	1 (1.5)	1 (1.5)
インフルエンザ	0	8 (12.3)	8 (12.3)
喉頭炎	0	1 (1.5)	1 (1.5)
限局性感染	0	1 (1.5)	1 (1.5)
下気道感染	0	2 (3.1)	2 (3.1)
肺感染	0	1 (1.5)	1 (1.5)
上咽頭炎	1 (25.0)	20 (30.8)	20 (30.8)
口腔真菌感染	0	2 (3.1)	2 (3.1)
口腔ヘルペス	0	5 (7.7)	5 (7.7)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
感染症および寄生虫症 (Cont.)	2 (50.0)	48 (73.8)	48 (73.8)
外耳炎	0	1 (1.5)	1 (1.5)
腹膜炎	0	2 (3.1)	2 (3.1)
百日咳	0	1 (1.5)	1 (1.5)
咽頭炎	0	4 (6.2)	4 (6.2)
レンサ球菌性咽頭炎	0	1 (1.5)	1 (1.5)
咽頭扁桃炎	0	1 (1.5)	1 (1.5)
気道感染	0	2 (3.1)	2 (3.1)
鼻炎	0	6 (9.2)	6 (9.2)
副鼻腔炎	0	5 (7.7)	5 (7.7)
皮膚感染	0	1 (1.5)	1 (1.5)
皮下組織膿瘍	0	1 (1.5)	1 (1.5)
頭部白癬	0	1 (1.5)	1 (1.5)
扁桃炎	0	2 (3.1)	2 (3.1)
歯膿瘍	0	5 (7.7)	5 (7.7)
気管炎	0	4 (6.2)	4 (6.2)
上気道感染	1 (25.0)	7 (10.8)	7 (10.8)
尿路感染	0	9 (13.8)	9 (13.8)
腟感染	0	1 (1.5)	1 (1.5)
ウイルス性咽頭炎	0	1 (1.5)	1 (1.5)
ウイルス性上気道感染	0	1 (1.5)	1 (1.5)
外陰部炎	0	1 (1.5)	1 (1.5)
外陰部腟カンジダ症	0	1 (1.5)	1 (1.5)
外陰腟真菌感染	0	2 (3.1)	2 (3.1)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
傷害、中毒および処置合併症	0	20 (30.8)	20 (30.8)
吻合部漏出	0	1 (1.5)	1 (1.5)
足関節部骨折	0	1 (1.5)	1 (1.5)
節足動物咬傷	0	1 (1.5)	1 (1.5)
結腸損傷	0	1 (1.5)	1 (1.5)
挫傷	0	5 (7.7)	5 (7.7)
転倒	0	4 (6.2)	4 (6.2)
前腕骨折	0	1 (1.5)	1 (1.5)
手骨折	0	1 (1.5)	1 (1.5)
股関節部骨折	0	1 (1.5)	1 (1.5)
瘢痕ヘルニア	0	1 (1.5)	1 (1.5)
靭帯捻挫	0	2 (3.1)	2 (3.1)
処置後合併症	0	2 (3.1)	2 (3.1)
処置後挫傷	0	1 (1.5)	1 (1.5)
処置による疼痛	0	1 (1.5)	1 (1.5)
交通事故	0	1 (1.5)	1 (1.5)
皮膚裂傷	0	1 (1.5)	1 (1.5)
熱傷	0	1 (1.5)	1 (1.5)
手首関節骨折	0	2 (3.1)	2 (3.1)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
臨床検査	1 (25.0)	17 (26.2)	17 (26.2)
アラニンアミノトランスフェラーゼ増加	0	4 (6.2)	4 (6.2)
大動脈雑音	0	1 (1.5)	1 (1.5)
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (3.1)	2 (3.1)
血中アルカリホスファターゼ増加	0	2 (3.1)	2 (3.1)
血中コレステロール増加	0	1 (1.5)	1 (1.5)
血中クレアチンホスホキナーゼ増加	0	3 (4.6)	3 (4.6)
血中クレアチニン増加	0	1 (1.5)	1 (1.5)
血中ブドウ糖増加	0	1 (1.5)	1 (1.5)
血中トリグリセリド増加	0	1 (1.5)	1 (1.5)
血中尿素増加	0	1 (1.5)	1 (1.5)
体温上昇	0	1 (1.5)	1 (1.5)
C－反応性蛋白増加	0	3 (4.6)	3 (4.6)
心雑音	0	1 (1.5)	1 (1.5)
腎クレアチニン・クリアランス増加	0	1 (1.5)	1 (1.5)
便中カルプロテクチン増加	0	1 (1.5)	1 (1.5)
γ－グルタミルトランスフェラーゼ増加	0	2 (3.1)	2 (3.1)
リパーゼ増加	0	1 (1.5)	1 (1.5)
肝機能検査値上昇	0	1 (1.5)	1 (1.5)
血清フェリチン増加	0	1 (1.5)	1 (1.5)
ビタミンB12減少	0	1 (1.5)	1 (1.5)
ビタミンD減少	0	1 (1.5)	1 (1.5)
体重減少	0	2 (3.1)	2 (3.1)
体重増加	1 (25.0)	2 (3.1)	2 (3.1)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
代謝および栄養障害	1 (25.0)	7 (10.8)	8 (12.3)
食欲減退	0	1 (1.5)	1 (1.5)
高血糖	0	1 (1.5)	1 (1.5)
鉄欠乏	0	2 (3.1)	2 (3.1)
ビタミンB12欠乏	1 (25.0)	2 (3.1)	3 (4.6)
ビタミンD欠乏	0	4 (6.2)	4 (6.2)
筋骨格系および結合組織障害	0	25 (38.5)	25 (38.5)
関節痛	0	11 (16.9)	11 (16.9)
関節炎	0	2 (3.1)	2 (3.1)
アレルギー性関節炎	0	1 (1.5)	1 (1.5)
関節障害	0	1 (1.5)	1 (1.5)
背部痛	0	8 (12.3)	8 (12.3)
滑液包炎	0	1 (1.5)	1 (1.5)
外骨腫	0	1 (1.5)	1 (1.5)
線維筋痛	0	1 (1.5)	1 (1.5)
関節硬直	0	1 (1.5)	1 (1.5)
筋痙縮	0	2 (3.1)	2 (3.1)
筋攣縮	0	1 (1.5)	1 (1.5)
筋骨格痛	0	2 (3.1)	2 (3.1)
筋骨格硬直	0	1 (1.5)	1 (1.5)
筋肉痛	0	5 (7.7)	5 (7.7)
頚部痛	0	2 (3.1)	2 (3.1)
骨減少症	0	1 (1.5)	1 (1.5)
四肢痛	0	5 (7.7)	5 (7.7)
足底筋膜炎	0	1 (1.5)	1 (1.5)
脊椎痛	0	1 (1.5)	1 (1.5)
滑膜炎	0	1 (1.5)	1 (1.5)
腱障害	0	3 (4.6)	3 (4.6)
腱炎	0	1 (1.5)	1 (1.5)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	4 (6.2)	4 (6.2)
肛門性器疣贅	0	1 (1.5)	1 (1.5)
大腸腺腫	0	1 (1.5)	1 (1.5)
メラノサイト性母斑	0	1 (1.5)	1 (1.5)
皮膚乳頭腫	0	2 (3.1)	2 (3.1)
神経系障害	0	20 (30.8)	20 (30.8)
頚動脈洞症候群	0	1 (1.5)	1 (1.5)
群発頭痛	0	1 (1.5)	1 (1.5)
複合性局所疼痛症候群	0	1 (1.5)	1 (1.5)
浮動性めまい	0	3 (4.6)	3 (4.6)
頭痛	0	9 (13.8)	9 (13.8)
嗜眠	0	1 (1.5)	1 (1.5)
片頭痛	0	3 (4.6)	3 (4.6)
後頭神経痛	0	1 (1.5)	1 (1.5)
安静時振戦	0	1 (1.5)	1 (1.5)
坐骨神経痛	0	1 (1.5)	1 (1.5)
緊張性頭痛	0	1 (1.5)	1 (1.5)
精神障害	0	11 (16.9)	11 (16.9)
不安	0	2 (3.1)	2 (3.1)
うつ病	0	2 (3.1)	2 (3.1)
不眠症	0	5 (7.7)	5 (7.7)
気分動揺	0	1 (1.5)	1 (1.5)
神経過敏	0	1 (1.5)	1 (1.5)
睡眠障害	0	1 (1.5)	1 (1.5)
ストレス	0	2 (3.1)	2 (3.1)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
腎および尿路障害	0	4 (6.2)	4 (6.2)
血尿	0	1 (1.5)	1 (1.5)
排尿異常	0	1 (1.5)	1 (1.5)
尿意切迫	0	1 (1.5)	1 (1.5)
頻尿	0	1 (1.5)	1 (1.5)
腎機能障害	0	1 (1.5)	1 (1.5)
尿失禁	0	1 (1.5)	1 (1.5)
生殖系および乳房障害	0	6 (9.2)	6 (9.2)
勃起不全	0	1 (1.5)	1 (1.5)
月経過多	0	1 (1.5)	1 (1.5)
小乳房	0	1 (1.5)	1 (1.5)
卵巣嚢胞	0	1 (1.5)	1 (1.5)
腟出血	0	2 (3.1)	2 (3.1)
外陰腟そう痒症	0	1 (1.5)	1 (1.5)
呼吸器、胸郭および縦隔障害	0	13 (20.0)	13 (20.0)
喘息	0	1 (1.5)	1 (1.5)
咳嗽	0	6 (9.2)	6 (9.2)
鼻出血	0	3 (4.6)	3 (4.6)
鼻閉塞	0	1 (1.5)	1 (1.5)
口腔咽頭痛	0	3 (4.6)	3 (4.6)
胸水	0	1 (1.5)	1 (1.5)
アレルギー性鼻炎	0	1 (1.5)	1 (1.5)
副鼻腔障害	0	1 (1.5)	1 (1.5)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
皮膚および皮下組織障害	0	19 (29.2)	19 (29.2)
脱毛症	0	3 (4.6)	3 (4.6)
水疱性皮膚炎	0	1 (1.5)	1 (1.5)
接触皮膚炎	0	1 (1.5)	1 (1.5)
皮膚乾燥	0	2 (3.1)	2 (3.1)
湿疹	0	3 (4.6)	3 (4.6)
紅斑	0	3 (4.6)	3 (4.6)
多汗症	0	1 (1.5)	1 (1.5)
光線過敏性反応	0	2 (3.1)	2 (3.1)
そう痒症	0	5 (7.7)	5 (7.7)
アレルギー性そう痒症	0	1 (1.5)	1 (1.5)
乾癬	0	1 (1.5)	1 (1.5)
発疹	0	4 (6.2)	4 (6.2)
紅斑性皮疹	0	1 (1.5)	1 (1.5)
丘疹性皮疹	0	1 (1.5)	1 (1.5)
酒さ	0	1 (1.5)	1 (1.5)
皮膚亀裂	0	1 (1.5)	1 (1.5)
蕁麻疹	0	1 (1.5)	1 (1.5)
外科および内科処置	0	1 (1.5)	1 (1.5)
選択的妊娠中絶	0	1 (1.5)	1 (1.5)
血管障害	0	7 (10.8)	7 (10.8)
血腫	0	1 (1.5)	1 (1.5)
出血	0	1 (1.5)	1 (1.5)
高血圧	0	3 (4.6)	3 (4.6)
低血圧	0	1 (1.5)	1 (1.5)
静脈瘤	0	1 (1.5)	1 (1.5)
血管炎	0	1 (1.5)	1 (1.5)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表4

[redacted]20[redacted] 01:32 <[redacted] >
RISANKIZUMAB (CROHN'S)
M15-989 ABBREVIATED CLINICAL STUDY REPORT
R&D/19/0019 - CLINICAL/STATISTICAL

TABLE 14.3__2.1.1

Subjects with Treatment-Emergent Serious Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
Any adverse event	0	23 (35.4)	23 (35.4)
血液およびリンパ系障害	0	1 (1.5)	1 (1.5)
鉄欠乏性貧血	0	1 (1.5)	1 (1.5)
心臓障害	0	1 (1.5)	1 (1.5)
頻脈	0	1 (1.5)	1 (1.5)
内分泌障害	0	1 (1.5)	1 (1.5)
副腎機能不全	0	1 (1.5)	1 (1.5)
胃腸障害	0	10 (15.4)	10 (15.4)
上腹部痛	0	1 (1.5)	1 (1.5)
クローン病	0	2 (3.1)	2 (3.1)
ダンピング症候群	0	1 (1.5)	1 (1.5)
痔核	0	1 (1.5)	1 (1.5)
回腸狭窄	0	1 (1.5)	1 (1.5)
イレウス	0	1 (1.5)	1 (1.5)
胃排出不全	0	1 (1.5)	1 (1.5)
腸閉塞	0	1 (1.5)	1 (1.5)
腸管狭窄	0	2 (3.1)	2 (3.1)
臍ヘルニア	0	1 (1.5)	1 (1.5)
一般・全身障害および投与部位の状態	0	1 (1.5)	1 (1.5)
胸痛	0	1 (1.5)	1 (1.5)
免疫系障害	0	1 (1.5)	1 (1.5)
アナフィラキシー反応	0	1 (1.5)	1 (1.5)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3__2.1.1

Subjects with Treatment-Emergent Serious Adverse Events
by System Organ Class and Preferred Term
(Safety Analysis Set)

MedDRA 21.1 System Organ Class Preferred Term	Risankizumab 600 mg IV Q4W (N=4) n (%)	Risankizumab 180 mg SC Q8W (N=65) n (%)	All Risankizumab (N=65) n (%)
感染症および寄生虫症	0	6 (9.2)	6 (9.2)
肛門膿瘍	0	1 (1.5)	1 (1.5)
カンピロバクター感染	0	1 (1.5)	1 (1.5)
ウイルス性胃腸炎	0	2 (3.1)	2 (3.1)
腹膜炎	0	2 (3.1)	2 (3.1)
皮下組織膿瘍	0	1 (1.5)	1 (1.5)
傷害、中毒および処置合併症	0	6 (9.2)	6 (9.2)
吻合部漏出	0	1 (1.5)	1 (1.5)
足関節部骨折	0	1 (1.5)	1 (1.5)
転倒	0	1 (1.5)	1 (1.5)
股関節部骨折	0	1 (1.5)	1 (1.5)
処置後合併症	0	2 (3.1)	2 (3.1)
処置による疼痛	0	1 (1.5)	1 (1.5)
熱傷	0	1 (1.5)	1 (1.5)
神経系障害	0	2 (3.1)	2 (3.1)
頚動脈洞症候群	0	1 (1.5)	1 (1.5)
群発頭痛	0	1 (1.5)	1 (1.5)
浮動性めまい	0	1 (1.5)	1 (1.5)
生殖系および乳房障害	0	2 (3.1)	2 (3.1)
月経過多	0	1 (1.5)	1 (1.5)
卵巣嚢胞	0	1 (1.5)	1 (1.5)
呼吸器、胸郭および縦隔障害	0	1 (1.5)	1 (1.5)
鼻閉塞	0	1 (1.5)	1 (1.5)
外科および内科処置	0	1 (1.5)	1 (1.5)
選択的妊娠中絶	0	1 (1.5)	1 (1.5)

Note: Treatment-Emergent adverse events are defined as events that begin or worsen either on or after the first dose of the study drug in the current study and within 140 days after the last dose administration of the study drug in the current study or until the first dose of the study drug of M16-000 sub-study 3 if the subject is enrolled into M16-000 sub-study 3. Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]