NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
NOT REPORTED

AE Stopped Rx Day	22 (21 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted] 20[redacted]:12:37
Program Source Code: [redacted]

20[redacted] 年[redacted] 月[redacted] 日に入手した[redacted]からの報告（参照番号：[redacted]）。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

スペインの実施医療機関番号[redacted] の治験責任医師から，被験者番号[redacted] に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病の 6[redacted]歳女性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第 II 相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

20[redacted] 年[redacted] 月[redacted] 日の 11 時 20 分から 12 時 20 分，治験薬の投与が行われた。

投与 19 日後，被験者は，軽度の腎前性腎不全，低浸透圧性（電解質失調）低ナトリウム血症及び中等度の代謝性アシドーシス（いずれも入院のため重篤と判断された）と診断された。投与から約 1 か月後，被験者は入院した。静脈内補液，イオン（マグネシウム及びカルシウム）補充，及び Bi-carbonate の投与による治療が行われた。入院の翌日，被験者の全身状態に著しい改善，良好な利尿，血清クレアチニンの正常化及び排便回数の減少が認められた。血清療法が中止され，被験者はイオン補充を継続した。投与 22 日後，被験者は事象から回復した。

追跡調査時，治験責任医師は，電解質失調が個別の事象ではなく，低浸透圧性低ナトリウム血症と同事象であることを確認した。

治験薬の治療状況は「該当なし」であった。

併用薬は，抗血小板薬として Adiro 及びクロピドグレル，クローン病に対する Metotrexato，予防目的の Acpol，抗高血圧薬（高血圧）としてエナラプリル，プロトンポンプ阻害薬としてオメプラゾール，並びにコレステロールに対する Atorvastatine であった。その他の合併症は報告されなかった。前治療として，クローン病に対するアダリムマブ及びインフリキシマブの投与歴があった。その他の既往歴は報告されなかった。

治験責任医師は，治験薬と軽度の腎不全，低浸透圧性低ナトリウム血症及び代謝性アシドーシスとの因果関係は「関連なし」と考える。これらの事象の他の考えられる原因として，疾患進行が報告された。

規制当局への報告目的で，ベーリンガーインゲルハイムは，軽度の腎不全，低浸透圧性低ナトリウム血症及び代謝性アシドーシスと治験薬との因果関係に「合理的な可能性がない」と評価した。

投与 253 日後，本治験の中間非盲検化が行われた。

投与 605 日後，治験実施計画書に規定の判定委員会のレビュー時，既に報告された重篤事象である軽度の腎不全の発現日を投与 19 日後とする結果を受領した。慎重なレビューの結果，本委員会は，軽度の腎不全が心血管イベントではなかったことを確認した。

投与 708 日後，治験実施計画書に規定の判定委員会のレビュー時，既に報告された重篤事象である軽度の腎不全の発現日を投与 19 日後とする結果を受領した。慎重なレビューの結果，本委員会は，軽度の腎不全が心血管イベントではなかったことを確認した。

Causality for ABBV-066 (blinded)

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1) Event of RENAL FAILURE MILD

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

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

2) Event of HYPONATREMIA [HYPO-OSMOLAR]

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

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

3) Event of METABOLIC ACIDOSIS

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

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

4) Event of [HYPONATREMIA] HYPO-OSMOLAR

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

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

Alternative Etiology for ABBV-066 (blinded)

_____

Event of RENAL FAILURE MILD

AbbVie: Event is more likely related to exacerbation of pre-existing Crohn's disease that resulted in dehydration leading to renal failure.

Event of HYPONATREMIA [HYPO-OSMOLAR]

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

Event of METABOLIC ACIDOSIS

AbbVie: Event is more likely related to renal failure.

Event of [HYPONATREMIA] HYPO-OSMOLAR

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

被験者番号[redacted] (Site[redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:RISA 200 MG IV / P2:RISA 600 MG IV	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANXIETY	Not reported.
ASTHENIA	Not reported.
EXTERNAL HEMORRHOID	Not reported.
FATIGUE	Not reported.
HYPOTIROIDISM	Not reported.
ILEAL RESECTION AND HEMICOLECTOMY	Not reported.
MIELOTOXICITY	Not reported.
TIROIDECTOMY	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	20[redacted]

Prior Procedures	Procedure Year
BIOPSY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO		Not reported.	Not reported.	Not reported.

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 100	[redacted]20[redacted] / 156	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	40 mg	1 TIME PER WEEK	Y-M: 20[redacted]-[redacted]
METHOTREXATE	20 mg	Not reported.	Y-M: 20[redacted]-[redacted] / -222

INFLIXIMAB	10 mg/kg	NOT APPLICABLE	Y-M: 20[redacted] / -163

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
FLUOXETINE HYDROCHLORIDE	Not reported.	Not reported.	Not reported.	Not reported.
FOLIC ACID	Not reported.	Not reported.	Not reported.	Not reported.
LEVOTHYROXINE SODIUM	Not reported.	Not reported.	Not reported.	Not reported.
OMEPRAZOLE	Not reported.	Not reported.	Not reported.	Not reported.
METHOTREXATE	20 mg	Not reported.	Y-M: 20[redacted] / -222	Not reported.
CELECOXIB	Not reported.	Not reported.	Y-M: 20[redacted] / 150	Not reported.
DIAZEPAM	Not reported.	Not reported.	Y-M: 20[redacted] / 178	Not reported.
VEDOLIZUMAB	300 mg	Not reported.	Y-M: 20[redacted] / 191	Not reported.
SALBUTAMOL	Not reported.	Not reported.	Y-M: 20[redacted] / 214	Not reported.
ENOXAPARIN SODIUM	Not reported.	Not reported.	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 238
METAMIZOLE MAGNESIUM	Not reported.	Not reported.	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 238
MICONAZOLE NITRATE	Not reported.	Not reported.	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 243

Event #1: Serious Adverse Event

Event Description	INTESTINAL SUBOCCLUSION
Preferred term	腸閉塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 234 (78 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	238 (82 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted] 20[redacted]:12:37
Program Source Code: [redacted]

20[redacted] 年[redacted] 月[redacted] 日に入手した[redacted]からの報告（参照番号：[redacted]）。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

スペインの実施医療機関番号[redacted] の治験責任医師から，被験者番号[redacted] に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病（20[redacted] 年[redacted]月[redacted] 日～）の 3[redacted] 歳女性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第II相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

20[redacted] 年[redacted] 月[redacted] 日，治験薬の投与が開始され，投与 156 日後に中止された。

投与 234 日後，被験者は，入院を要したため重篤と判断された重度の亜腸閉塞を発現した。被験者は嘔吐し始め，便沈着及び腹痛があった。被験者は救急科を受診し，亜腸閉塞と診断され，入院した。亜腸閉塞に対する治療として，血清療法，オメプラゾール及び頓用（PRN）Metamizole の投与が行われた。投与 234 日後から投与 238 日後まで，血栓症予防の目的で Enoxaparine の皮下（SC）投与も行われた。投与 238 日後，被験者は亜腸閉塞から回復し，同日，退院した。

被験者は，本事象の発現時に治療を中止していたため，本事象後の治験薬の治療状況は「該当なし」であった。

併用薬は，甲状腺機能低下症（19[redacted] 年～）に対する Eutirox，不安（20[redacted] 年[redacted] 月～）に対するフルオキセチン，胃の保護目的のオメプラゾール，葉酸欠乏症予防目的の葉酸，クローン病（20[redacted] 年[redacted] 月[redacted] 日～）に対するメトトレキサート及びベドリズマブ，クローン病による腹痛に対する Metamizole，並びに気管支過敏症（20[redacted] 年[redacted]月[redacted] 日～）に対する Salbutamol であった。その他の合併症は，外痔核，無力症及び疲労であった。既往歴は，回腸切除及び半結腸切除，並びに骨髄毒性及び甲状腺摘除であった。

治験責任医師は，治験薬と亜腸閉塞との因果関係は「関連なし」と考える。

規制当局への報告目的で，ベーリンガーインゲルハイムは，亜腸閉塞と治験薬との因果関係に「合理的な可能性がない」と評価した。

投与 526 日後，本治験が非盲検化され，被験者は治療の盲検期に BI 655066 200 mg iv に割り付けられたが，本事象（亜腸閉塞）の発現時，被験者が直近で受けた用量は非盲検 BI 655066 600 mg iv であった。

Causality for ABBV-066 (blinded)

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1) INTESTINAL SUBOCCLUSION

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

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

Alternative Etiology for ABBV-066 (blinded)

Event of INTESTINAL SUBOCCLUSION

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

被験者番号[redacted] (Site[redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
DEPRESSION	Not reported.
DEVELOPMENTAL ACADEMIC DISORDER (NO INFO)	Not reported.
ECZEMA	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	19[redacted]

Prior Procedures	Procedure Year
BIOPSY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

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

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SERTRALINE	Not reported.	Not reported.	Not reported.	Not reported.
PREDNISOLONE	25 mg	Not reported.	Y-M: 20[redacted]-[redacted] / 6	Not reported.

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

Event Description	EXCERBATION OF CROHNS DISEASE
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 6 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	7 (6 DAYS AFTER LAST TREATMENT)
Duration of AE	2 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:12:37
Program Source Code: [redacted]

20[redacted]年[redacted]月[redacted]日に入手した[redacted]からの報告（参照番号：[redacted]）。

英国の実施医療機関番号[redacted]の治験責任医師から，被験者番号[redacted]に関する情報を入手した。本被験者は，19[redacted]年に中等度から重度の活動性クローン病と診断された2[redacted]歳女性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第Ⅱ相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

20[redacted]年[redacted]月[redacted]日の 11 時 37 分から 13 時 9 分まで，治験薬の単回投与が行われた。

投与 6 日後，被験者は，入院のため重篤と判断されたクローン病増悪を発現した。被験者は，腹痛，嘔吐及び血性下痢の関連症状のため救急救命（A&E）科に入院した。C－反応性蛋白

（CRP）が 154 まで増加し，被験者は，発熱及び脳灌流圧（CPP）上昇（CPP: 180）も発現した。被験者は，ヒドロコルチゾンの静脈内投与，Co-Codamol 及び Oramorph＋静脈内輸液の投与を開始し，いずれの薬剤も被験者の症状を緩和した。被験者は，クローン病のフレアの疑い及び／又は薬剤反応の可能性を発現した。治験薬は本事象発現 5 日前に投与されたため，治験薬の投与が事象発現を予防した可能性は低い。投与 7 日後，被験者はクローン病増悪から回復し，同日，退院時に経口コルチコステロイドを処方された。

投与 85 日後，被験者は，回腸瘻造設のため待機的入院をした。被験者は，試験開腹及びループ状回腸瘻造設のため入院し，予定通り手術が行われた。本報告時点で，被験者は入院中であった。

投与 12 日後，クローン病増悪の事象後に患者がリスクにさらされることがないよう，治験薬の投与を永続的に中止した。本事象後，治験薬の治療状況は「該当なし」であった。

併用薬及び合併症は報告されなかった。

治験責任医師は，治験薬とクローン病増悪との因果関係は「関連あり」と考える。

規制当局への報告目的で，ベーリンガーインゲルハイムは，治験薬とクローン病増悪との因果関係に「合理的な可能性がない」と評価した。

被験者番号[redacted](Site[redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
ACHALASIA	Not reported.
BACK AND LEG PAIN	Not reported.
BRONCHIECTASIS	Not reported.
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	Not reported.
EPICONDYLITIS	Not reported.
LICHEN SCLEROSUS	Not reported.
OSTEOARTHRITIS	Not reported.
OSTEOPOROSIS	Not reported.
PERIORBITAL ERYTHEMA	Not reported.
SIGMOID COLECTOMY	Not reported.
SWEET'S SYNDROME	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	20[redacted]

Prior Procedures	Procedure Year
SURGERIES FOR TRIAL DISEASE: SIGMOID COLECTOMY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Not reported.

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]0[redacted] / 1	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
Not reported.			

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CALCIUM CARBONATE	Not reported.	Not reported.	Not reported.	Not reported.
ESOMEPRAZOLE	Not reported.	Not reported.	Not reported.	Not reported.
FERROUS SULFATE	Not reported.	Not reported.	Not reported.	Not reported.
INFLIXIMAB	Not reported.	EVERY 6 WEEKS	Not reported.	Not reported.
PREDNISOLONE	20 mg	Not reported.	Not reported.	Not reported.

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

Event Description	EXACERBATION OF CROHNS DISEASE
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted] / 27 (26 DAYS AFTER LAST TREATMENT)
Age at AE Onset	[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	36 (35 DAYS AFTER LAST TREATMENT)
Duration of AE	10 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]:12:37
Program Source Code: [redacted]

[redacted]年[redacted]月[redacted]日に入手した[redacted]からの報告（参照番号：[redacted]）。

アイルランドの実施医療機関番号[redacted]の治験責任医師から，被験者番号[redacted]に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病の[redacted]歳女性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第 II

相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

20[redacted] 年[redacted] 月[redacted] 日の 12 時 45 分から 14 時 33 分まで，治験薬の（初回）投与が行われた。

投与 23 日後，被験者は，クリニックの医師の診察を受け，敗血症の予防としてシプロフロキサシンの経口投与が開始された。投与 27 日後，被験者は，グレード 3 のクローン病増悪を発現し，入院した。本報告日から過去 3 日間にわたり，症状が悪化した。症状は，排便回数増加，進行性直腸痛，発熱，食欲不振及び体重減少であった。投与 27 日後，S 状結腸鏡検査が行われ，S 状結腸に潰瘍が認められた。症状の悪化が持続した結果，被験者は治験参加を中止した。入院は，ステロイドの静脈内投与による治療のためであった。

投与 36 日後，被験者はクローン病増悪から回復した。

治験薬の投与は中止された。

併用薬は，敗血症の予防目的のシプロフロキサシン，試験対象疾患（クローン病）に対するプレドニゾロン，胃逆流に対するエソメプラゾール及び炭酸カルシウム（使用理由不明）であった。その他の合併症は報告されなかった。前治療として，Co-codamol（使用理由不明）の投与歴があった。既往歴は，背部痛及び下肢痛，眼窩周囲紅斑，外陰部硬化性苔癬，Sweet 症候群，骨粗鬆症，変形性関節症，気管支拡張症，並びに慢性閉塞性肺疾患であった。

治験責任医師は，治験薬とクローン病増悪との因果関係は「関連あり」と考える。

規制当局への報告目的で，ベーリンガーインゲルハイムは，クローン病増悪と治験薬との因果関係に「合理的な可能性がない」と評価した。

被験者番号[redacted] (Site[redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:RISA 600 MG IV / P2:RISA 600 MG IV	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ANEMIA	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	20[redacted]

Prior Procedures	Procedure Year
BIOPSY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Not reported.

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 99	[redacted]20[redacted] / 155	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	400 mg	EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
MEROKEN NEW	Not reported.	Not reported.	Y-M: 20[redacted]-[redacted] / -13

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	Not reported.	Not reported.	Y-M: 20[redacted]-[redacted] / 76	Y-M: 20[redacted]-[redacted] / 76

PARACETAMOL	Not reported.	Not reported.	Y-M: 20[redacted] / 107 Y-M: 20[redacted] / 107
FENTANYL	Not reported.	Not reported.	Y-M: 20[redacted] / 108 Y-M: 20[redacted] / 108
MIDAZOLAM	Not reported.	Not reported.	Y-M: 20[redacted] / 108 Y-M: 20[redacted] / 108
MEROKEN NEW	Not reported.	Not reported.	Y-M: 20[redacted] / 108 Y-M: 20[redacted] / 111
METRONIDAZOLE	Not reported.	Not reported.	Y-M: 20[redacted] / 147 Y-M: 20[redacted] / 161
FLUCLOXACILLIN	Not reported.	Not reported.	Y-M: 20[redacted] / 177 Not reported.
FERRIC CARBOXYMALTOSE	Not reported.	Not reported.	Y-M: 20[redacted] / 183 Y-M: 20[redacted] / 183
VITAMIN B12 NOS	Not reported.	Not reported.	Y-M: 20[redacted] / 183 Y-M: 20[redacted] / 183

Event #1: Serious Adverse Event

Event Description	WORSENING OF CROHN'S DISEASE
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 105
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	260 (105 DAYS AFTER LAST TREATMENT)
Duration of AE	156 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:12:37
Program Source Code: [redacted]

20[redacted]年[redacted]月[redacted]日に入手した[redacted]からの報告（参照番号：[redacted]）。

英国の実施医療機関番号 [redacted] の治験責任医師から，被験者番号 [redacted] に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病の 3[redacted] 歳男性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第 II 相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

20[redacted] 年[redacted] 月[redacted] 日の 13 時 20 分から 15 時 15 分まで，治験薬の投与が行われた。

投与 105 日後の 8 時 0 分，被験者は，入院のため重篤と判断されたクローン病悪化を発現した。被験者は，クローン病悪化のためクリニックから入院した。被験者は，腹痛の増強があり，本事象に対して静脈内（IV）輸液の投与を受けた。被験者は，クローン病悪化から回復していなかった。

治験薬の投与は継続された。

併用薬及び合併症は「なし」と報告された。

治験責任医師は，クローン病悪化と治験薬との因果関係は「関連あり」と考える。クローン病は，治験薬投与後 1 週間以内に悪化した。

規制当局への報告目的で，ベーリンガーインゲルハイムは，クローン病悪化と治験薬との因果関係に「合理的な可能性がある」と評価した。

被験者番号[redacted] (Site[redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:RISA 200 MG IV	5[redacted]	FEMALE	ASIAN

Medical History	Onset Year
DEPRESSION	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	19[redacted]

Prior Procedures	Procedure Year
BIOPSY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 26	26

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	40 mg	1 TIME PER WEEK	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	EVERY 8 WEEKS	Y-M: 20[redacted]
FERROUS SULFATE	Not reported.	Not reported.	Y-M: 20[redacted] / -51

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LOPERAMIDE HYDROCHLORIDE	2 mg	Not reported.	Not reported.	Not reported.
PARACETAMOL	Not reported.	Not reported.	Not reported.	Not reported.

PREDNISOLONE	10 mg	Not reported.	Not reported.	Not reported.
SERTRALINE	Not reported.	Not reported.	Not reported.	Y-M: 20[redacted] / 21
INFLIXIMAB	5 mg/kg	EVERY 8 WEEKS	Y-M: 20[redacted]	Not reported.
FERROUS SULFATE	Not reported.	Not reported.	Y-M: 20[redacted] / -51	Y-M: 20[redacted] / 27
LACTULOSE	Not reported.	Not reported.	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 27

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

Event Description	PERFERATED BOWEL
Preferred term	腸管穿孔
AE Onset Date / Rx Day	[redacted]20[redacted] / 29 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	30 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	2 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:12:37
Program Source Code: [redacted]

20[redacted]年[redacted]月[redacted]日に入手した[redacted]からの報告（参照番号：[redacted]）。

英国の実施医療機関番号[redacted]の治験責任医師から，被験者番号[redacted]に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病（19[redacted]年[redacted]月[redacted]日～）の5[redacted]歳女性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第II相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

20[redacted] 年[redacted] 月[redacted] 日の 11 時 2 分から 12 時 40 分まで，治験薬の投与が行われた。

投与 29 日後の 12 時 20 分，被験者は，入院を要する腸管穿孔があった。被験者は，治験責任医師に連絡し発熱及び嘔吐を訴え，静脈内療法（IVT），中間尿（MSU）及び精密検査のため入院した。発熱に対して Paracetamol の静脈内投与が行われた。腹部のコンピュータ断層撮影（CT）スキャンの結果，重篤な限局性 S 状結腸穿孔が認められた。投与 30 日後の 16 時 0 分，結腸亜全摘除及び（腹腔鏡下）回腸切除が行われた。同日，被験者は腸管穿孔から回復した。

投与 35 日後，被験者は，流動食による軽い食事を摂ることができた。静脈内療法は中止された。現在，被験者は人工肛門を使用している。

治験薬の治療状況は「該当なし」であった。

併用薬は，「なし」と報告された。合併症は，うつ病（20[redacted] 年[redacted] 月[redacted] 日～）及び貧血であった。既往歴は，間質性肺疾患であった。

治験責任医師は，治験薬と腸管穿孔との因果関係は「関連なし」と考える。本有害事象は既知のクローン病と一致するため，治験薬と関連がある可能性が低いと報告された。

規制当局への報告目的で，ベーリンガーインゲルハイムは，腸管穿孔と治験薬との因果関係に「合理的な可能性がない」と評価した。

以下の BI 症例 ID は本被験者に関連付けられている：[redacted]。

投与 243 日後，本治験の中間非盲検化が行われた。

被験者番号[redacted] (Site[redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
一過性失明	X			

Treatment Group	Age at Study Start	Sex	Race
P1:RISA 200 MG IV / P2:RISA 600 MG IV / P3:RISA 180 MG SC	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
BICORNUATE UTERUS	Not reported.
FATIGUE	Not reported.
MIGRAINE	Not reported.
PERIANAL INFLAMMATION	Not reported.
PSORIASIS	Not reported.
RECURRENT MOUTH ULCERS	Not reported.
SINUS/NASAL INFECTIONS	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	20[redacted]

Prior Procedures	Procedure Year
BIOPSY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 101	[redacted]20[redacted] / 156	56
Risankizumab	180 mg	SC	Every 8 Weeks	[redacted]20[redacted] / 182	[redacted]20[redacted] / 351	170

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	Not reported.	Not reported.	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]

SUMATRIPTAN	Not reported.	Not reported.	Y-M: 20[redacted] / -62
VITAMIN D NOS	Not reported.	Not reported.	Y-M: 20[redacted] / -35
OSMOTICALLY ACTING LAXATIVES	Not reported.	Not reported.	Y-M: 20[redacted] / -19
SENNA ALEXANDRINA	Not reported.	Not reported.	Y-M: 20[redacted] / -19
FENTANYL	Not reported.	Not reported.	Y-M: 20[redacted] / -18
HYOSCINE BUTYLBROMIDE	Not reported.	Not reported.	Y-M: 20[redacted] / -18
MIDAZOLAM	Not reported.	Not reported.	Y-M: 20[redacted] / -18

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SUMATRIPTAN	Not reported.	Not reported.	Y-M: 20[redacted] / -62	Not reported.
VITAMIN D NOS	Not reported.	Not reported.	Y-M: 20[redacted] / -35	Not reported.
HYDROCORTISONE	Not reported.	Not reported.	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 128
FOLIC ACID	Not reported.	Not reported.	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 163
ERGOCALCIFEROL	Not reported.	Not reported.	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 168
HYDROCORTISONE	Not reported.	Not reported.	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 156

Event #1: Serious Adverse Event

Event Description	INTERMITTENT TRANSIENT BLINDNESS IN RT EYE
Preferred term	一過性失明
AE Onset Date / Rx Day	[redacted]20[redacted] / 153
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	244
Duration of AE	92 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

20[redacted] 年[redacted] 月[redacted] 日に入手した[redacted]からの報告（参照番号[redacted]）。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

英国の実施医療機関番号[redacted] の治験責任医師から，被験者番号[redacted]に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病の 4[redacted] 歳女性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第 II 相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

20[redacted] 年[redacted] 月[redacted] 日の 12 時 14 分から 20[redacted] 年[redacted] 月[redacted]日の 14 時 25 分まで，非盲検で治験薬（600 mg IV 注射を 4 週間ごと）の投与が行われ，20[redacted] 年[redacted] 月[redacted] 日の 14 時 10 分，治験薬（180 mg sc を 8 週間ごと）の投与が再開された。

投与 153 日後，被験者は，常に重篤な事象と判断される重度の一過性失明が右眼にあった。被験者は，右眼の視力喪失は時々朝に発現し，1 時間ほど継続していたと報告した。被験者は眼科医の診察を受け，眼科病院を紹介された。眼科医の診察では異常は認められなかった。一過性失明に対する治療は行われなかった。投与 214 日後，被験者は右眼の一過性失明から回復した。

不明日，被験者は眼科病院で診察を受け，両眼ともに問題はないと評価された。神経科医への紹介が提案された。被験者のかかりつけ医は，被験者の状況を把握していた。

投与 519 日後，被験者が視覚誘発電位検査を受けた結果，視覚誘発電位は正常・対称であり，重大な視覚路障害の所見は認められなかった。眼科医を受診するたびに誘発電位検査が行われ，結果は正常であった。このことから，視神経に持続的な損傷の所見はなかった。測定された視力は，両眼ともに 69 cm（眼鏡なし）で N4.5 であった。

不明日，被験者は，神経科医の診察を受けた。診断は下されなかった。被験者は，追加で脳の磁気共鳴画像（MRI），頭部の磁気共鳴血管造影（MRA）及び視覚誘発電（VEP）検査を受ける必要があった。

治験薬の投与は継続された。

併用薬は，片頭痛に対するスマトリプタンであった。合併症は報告されなかった。既往歴は，双角子宮，片頭痛，疲労，肛門周囲炎，乾癬，再発口腔内潰瘍及び副鼻腔／鼻腔感染であった。

治験責任医師は，治験薬と右眼の一過性失明との因果関係は「関連なし」と考える。因果関係の根拠は，片眼の一過性症状の視力喪失は説明することが困難であり，眼科医も確認できなかったことであった。被験者は治験薬の投与を継続して受け，症状は消失した。

規制当局への報告目的で，ベーリンガーインゲルハイムは，右眼の一過性失明と治験薬との因果関係に「合理的な可能性がない」と評価した。

投与 702 日後，治験実施計画書に規定の特に注目すべき有害事象（AESI）判定委員会のレビュー時，既に報告された右眼の一過性失明の発現日を投与 153 日後とする結果を受領した。慎重なレビューの結果，本委員会は，右眼の一過性失明が心イベントではなかったことを確認した。

Causality for ABBV-066

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1) INTERMITTENT TRANSIENT BLINDNESS IN RIGHT EYE

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

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

Alternative Etiology for ABBV-066

AbbVie: Event resolved while study drug administration was ongoing and uninterrupted suggests alternate etiology. Pre-existing migraine is a potential risk factor.

被験者番号[redacted] (Site[redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
循環虚脱	X			
不全片麻痺	X			
腸閉塞	X			

Treatment Group	Age at Study Start	Sex	Race
P1:RISA 600 MG IV / P2:RISA 600 MG IV / P3:RISA 180 MG SC	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
BILE SALT MALABSORPTION	Not reported.
DEPRESSION	Not reported.
DUODENAL ULCER	Not reported.
FIBROIDS	Not reported.
GILBERTS SYDROME	Not reported.
SPINAL DISC PROBLEM	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	20[redacted]

Prior Procedures	Procedure Year
BIOPSY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO	FORMER	Not reported.	Not reported.	Not reported.

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted] 20[redacted] / 1	[redacted] 20[redacted] / 57	57
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted] 20[redacted] / 99	[redacted] 20[redacted] / 157	59
Risankizumab	180 mg	SC	Every 8 Weeks	[redacted] 20[redacted] / 183	[redacted] 20[redacted] / 351	169

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	5 mg/kg	EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]

ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
CERTOLIZUMAB	400 mg	ONCE	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
CALCIUM CARBONATE	Not reported.	Not reported.	Not reported.	Not reported.
CITALOPRAM	Not reported.	Not reported.	Not reported.	Not reported.
COLESEVELAM	Not reported.	Not reported.	Not reported.	Not reported.
EPINEPHRINE	Not reported.	Not reported.	Not reported.	Not reported.
FOLIC ACID	Not reported.	Not reported.	Not reported.	Not reported.
LANSOPRAZOLE	Not reported.	Not reported.	Not reported.	Not reported.
PARACETAMOL	Not reported.	Not reported.	Not reported.	Not reported.
VITAMIN B12 NOS	Not reported.	Not reported.	Not reported.	Not reported.
CHLORPHENAMINE MALEATE	Not reported.	Not reported.	Y-M: 20[redacted] / 99	Y-M: 20[redacted] / 99
HYDROCORTISONE	Not reported.	Not reported.	Y-M: 20[redacted] / 99	Y-M: 20[redacted] / 99
CLOPIDOGREL	Not reported.	Not reported.	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 237
CHLORPHENAMINE MALEATE	Not reported.	Not reported.	Y-M: 20[redacted] / 239	Y-M: 20[redacted] / 239
HYDROCORTISONE	Not reported.	Not reported.	Y-M: 20[redacted] / 239	Y-M: 20[redacted] / 239
CHLORPHENAMINE MALEATE	Not reported.	Not reported.	Y-M: 20[redacted] / 302	Y-M: 20[redacted] / 302
HYDROCORTISONE	Not reported.	Not reported.	Y-M: 20[redacted] / 302	Y-M: 20[redacted] / 302
CODEINE PHOSPHATE	Not reported.	Not reported.	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 324

Event #1: Serious Adverse Event

Event Description	COLLAPSE WITHOUT LOSS OF CONCIOUSNESS
Preferred term	循環虚脱
AE Onset Date / Rx Day	[redacted]20[redacted] / 99
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	99
Duration of AE	1 DAY

Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	LEFT SIDED WEAKNESS
Preferred term	不全片麻痺
AE Onset Date / Rx Day	[redacted] / 218
Age at AE Onset	[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	302
Duration of AE	85 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	SUBACUTE OBSTRUCTION DUE TO STENOSIS - BOWEL
Preferred term	腸閉塞
AE Onset Date / Rx Day	[redacted] / 323
Age at AE Onset	[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	329
Duration of AE	7 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

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20[redacted] 年[redacted] 月[redacted] 日に入手した[redacted]からの報告（参照番号：[redacted]）。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

英国の実施医療機関番号[redacted]の治験責任医師から，被験者番号[redacted]に関する情報を入手した。本被験者は，クローン病（20[redacted] 年[redacted]月[redacted] 日～）の 4[redacted]歳女性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第 II 相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

被験者は，20[redacted] 年から椎間板に障害があった。

20[redacted] 年[redacted]月[redacted]日から 20[redacted] 年[redacted] 月[redacted] 日まで，治験薬の投与が行われた。20[redacted] 年[redacted] 月[redacted] 日から 20[redacted] 年[redacted]月[redacted]日まで及び 20[redacted] 年[redacted]月[redacted] 日，治験薬の再投与が行われた。

投与 218 日後，被験者は，グレード 2 の左側脱力を発現し，同日，入院した。左側脱力はリウマチ共通毒性基準（RCTC）でグレード 2 と評価された。初回臨床検査では左側脱力の病理所見は認められず，精密検査は保留となった。神経学的症状は被験者の神経学的問題と関連しないように考えられると報告された。投与 220 日後から，被験者はクロピドグレル 1 日用量 75 mg の投与を受けた。

投与 302 日後，身体検査で左側脱力は認められず，被験者は本事象から回復した。

治験薬の投与は継続された。

併用薬は，カルシウム補充目的の Calcichew，うつ病（20[redacted] 年に発症）に対する Citalopram，胆汁塩吸収不良（20[redacted] 年に発症）に対するコレセベラム，十二指腸潰瘍（20[redacted] 年に発症）に対するランソプラゾール，鎮痛療法として Paracetamol，葉酸サプリメントとして葉酸，栄養補助として Fortisip ジュース及び急性アナフィラキシーに対するエピペンであった。その他の合併症

は，椎間板障害（20[redacted]年～），子宮類線維症（20[redacted] 年[redacted] 月～）及びジルベール症候群（20[redacted] 年[redacted] 月[redacted] 日～）であった。

治験責任医師は，治験薬と左側脱力との因果関係は「関連なし」と考える。

規制当局への報告目的で，ベーリンガーインゲルハイムは，左側脱力と治験薬との因果関係に「合理的な可能性がない」と評価した。

以下の BI 症例 ID は本被験者に関連付けられている：[redacted]，[redacted]及び[redacted]。

投与 897 日後，治験実施計画書に規定の判定委員会のレビュー時，既に報告された重篤事象である左側脱力の発現日を投与 218 日後とする結果を受領した。慎重なレビューの結果，本委員会は，左側脱力が「評価不能」と判断した。委員会は，追加の日付，臨床所見及び／又は画像に関する詳細なしでは判定できなかった。本治験がクローズし，追加情報の入手ができなくなった。

Causality for ABBV-066 (Blinded)

Event of LEFT SIDED WEAKNESS

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

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

Alternative Etiology for ABBV-066 (Blinded)

Event of LEFT SIDED WEAKNESS

AbbVie: Based on the investigator's opinion and limited information received, Abbvie chooses to support the investigator's opinion of causality. Additional risk factor includes pre-existing spinal disc problems since 20[redacted].

20[redacted] 年[redacted] 月[redacted] 日に入手した[redacted]からの報告（参照番号：[redacted]）。

****注：**BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

英国の実施医療機関番号[redacted]の治験責任医師から，被験者番号[redacted]に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病（20[redacted]年[redacted]月[redacted]日）の4[redacted]歳女性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第II相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

20[redacted]年[redacted]月[redacted]日から 20[redacted]年[redacted]月[redacted]日まで，盲検治療として治験薬の投与が開始された。

20[redacted]年[redacted]月[redacted]日，被験者は，非盲検期（R1 来院）の治験薬初回投与を受けた。被験者は 2 時間観察下におかれ，16 時 30 分に退院した。

投与 99 日後，被験者は，入院のため重篤と判断された意識消失を伴わないグレード 1（軽度）の虚脱を発現した。病院にて，被験者は両脚が重く感じ，意識消失を伴わない虚脱状態があったと述べた。被験者は，頻脈及び高血圧傾向［血圧（BP）105/109 mmHg，脈拍（p）130/分，体温（T）37.5°C 及び呼吸数（R）21/分］にあった。本事象に対する治療は行われなかった。投与 99 日後（同日），被験者は意識消失を伴わない虚脱から回復した。被験者は観察目的で 1 晩入院した。退院要約から，被験者は治験薬の投与を受けた後に全身の不調を感じたため，投与 99 日後の午後に入院したことが明らかとなった。被験者は，脈が飛ぶように感じており，その頃には全身が脱力していると感じ，脚の力が抜けていた。被験者の血液が検査され，リン酸低値が認められたため，その後補充された。意識消失を伴なわず命にかかわらない虚脱があり，被験者は当時，わずかに頻脈及び低血圧傾向にあった。病棟への入院時，被験者の状態は良好であり，被験者は観察のみの目的で入院した。身体検査の結果，全体的に特記すべきことはなく，評価時の血圧及び心拍数は正常であった。その後，投与 101 日後に被験者は退院した。

投与 253 日後，退院証明書が提供され，退院時の診断は頸椎神経根障害／筋骨格（MSK）疼痛であることが判明した。MRI 検査の結果，心室は対称で，拡張は認められなかった。大脳の主要血管の flow void は正常であり，前方循環が優位（変化なし）であった。重大な白質疾患の所見はなく，FLAIR での高信号異常の所見もなかった。限定拡散の所見はなかった。急性又は慢性の脳卒中の所見はなかった。小脳，頭頸接合部，脳幹，下垂体及び交叉槽周辺の所見は正常であった。出血又は微小出血歴の所見はなかった。特定の頭蓋内異常は認められなかった。

投与 323 日後，被験者は，入院のため重篤と判断された亜急性閉塞があった。不明日，被験者は重度の腹痛及び機能障害があり，手術病棟に入院した。投与 324 日後，被験者がコンピュータ断層撮影（CT）スキャンを受けた結果，亜急性吻合部狭窄が認められた。本事象に対する治療は行われなかった。投与 329 日後，被験者は亜急性閉塞から回復した。

投与 353 日後，被験者は，入院のため重篤と判断された共通用語基準（CTC）グレード 2（中等度）の狭窄に起因する亜急性閉塞を発現した。本事象に対する治療が行われた（詳細不明）。投与 359 日後，被験者は狭窄に起因する亜急性閉塞から回復した。

治験薬の投与は継続された。

併用薬は，カルシウム補充目的の Calcichew，うつ病（20[redacted] 年～）に対する Citalopram，胆汁塩吸収不良（20[redacted] 年～）に対するコレセベラム，十二指腸潰瘍（20[redacted] 年～）に対するランソプラゾール，鎮痛療法として Paracetamol，葉酸サプリメントとして葉酸，栄養補助として Fortisip ジュース及び急性アナフィラキシーに対するエピペンであった。その他の合併症は，椎間板障害（20[redacted] 年～），子宮類線維症（20[redacted] 年[redacted] 月～）及びジルベール症候群（20[redacted] 年[redacted] 月[redacted] 日～）であった。

治験責任医師は，治験薬と意識消失を伴わない虚脱，亜急性閉塞及び狭窄に起因する亜急性閉塞との因果関係は「関連なし」と考える。被験者は MRI スキャンの前に CT スキャンを受けており，保存的治療によって症状が急速に消失したこと，回腸終端部の狭窄に起因する亜急性閉塞が原因である可能性が高いことが報告された。因果関係の根拠として，被験者は当日，非盲検で治験薬を受けることに対して非常に緊張していたことが報告された。被験者の症状は実際の生理学的な異常とは一致しなかった。医師の印象として，被験者の症状と意識消失を伴わない虚脱は，治験薬ではなく不安に関連していた。

規制当局への報告目的で，ベーリンガーインゲルハイムは，意識消失を伴わない虚脱，狭窄に起因する亜急性閉塞及び亜急性閉塞と治験薬との因果関係に「合理的な可能性がない」と評価した。

以下の BI 症例 ID は本被験者に関連付けられている：[redacted]。

投与 442 日後，本治験の中間非盲検化が行われた。

投与 794 日後，治験実施計画書に規定の判定委員会のレビュー時，既に報告された意識消失を伴わない虚脱の発現日を投与 99 日後とする結果を受領した。慎重なレビューの結果，本委員会は，上記事象が血栓イベントではなかったことを確認した。

Causality for ABBV-066 (Open-label)

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1) COLLAPSE WITHOUT LOSS OF CONCIOUSNESS

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

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

Alternative Etiology for ABBV-066 (Open-label)

Event of COLLAPSE WITHOUT LOSS OF CONCIOUSNESS

AbbVie: According to the investigator, the patient was very nervous on the day that she would receive the open label study medication. Furthermore as per PI, this event is more likely related to anxiety. Additionally, patient has pre-existing acute anaphylaxis.

Causality for ABBV-066 (Open-label)

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2) SUBACUTE OBSTRUCTION

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

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

Alternative Etiology for ABBV-066 (Open-label)

Event of SUBACUTE OBSTRUCTION

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

Causality for ABBV-066 (Open-label)

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2) SUBACUTE OBSTRUCTION DUE TO STENOSIS

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

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

Alternative Etiology for ABBV-066 (Open-label)

Event of SUBACUTE OBSTRUCTION DUE TO STENOSIS

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

All pertinent information from deleted case [redacted] has been entered into this report which will remain in the database.

Reference deleted case: [redacted]

被験者番号[redacted] (Site[redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:RISA 200 MG IV / P2:RISA 600 MG IV / P3:RISA 180 MG SC	2[redacted]	MALE	ASIAN

Medical History	Onset Year
PRIMARY DIAGNOSIS: CROHN"S DISEASE	20[redacted]

Prior Procedures	Procedure Year
BIOPSY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO		Not reported.	Not reported.	Not reported.

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 63	63
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 99	[redacted]20[redacted] / 155	57
Risankizumab	180 mg	SC	Every 8 Weeks	[redacted]20[redacted] / 197	[redacted]20[redacted] / 351	155

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
Not reported.			

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	1 mg	Not reported.	Not reported.	Not reported.
FOLIC ACID W/MINERALS NOS/VITAMINS NOS	600 mg	Not reported.	Not reported.	Not reported.

MERCAPTOPURINE	50 mg	Not reported.	Not reported.	Not reported.
METHYLPREDNISOLONE ACETATE	12 mg	Not reported.	Not reported.	Y-M: 20[redacted] / 231
IPRATROPIUM BROMIDE MONOHYDRATE	Not reported.	Not reported.	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 56
OSELTAMIVIR PHOSPHATE	Not reported.	Not reported.	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 56
SALBUTAMOL	Not reported.	Not reported.	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 56
PREDNISOLONE	Not reported.	Not reported.	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 57
AZITHROMYCIN	Not reported.	Not reported.	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 58
CODEINE PHOSPHATE	Not reported.	Not reported.	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 58
UNACID	Not reported.	Not reported.	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 58
BUDESONIDE W/FORMOTEROL FUMARATE	Not reported.	Not reported.	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 58

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted]:14:00 / 51
Age at AE Onset	[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	58
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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Program Source Code: [redacted]

20[redacted] 年[redacted] 月[redacted] 日に入手した[redacted]からの報告（参照番号：[redacted]）。

韓国の実施医療機関番号[redacted]の治験責任医師から，被験者番号[redacted] に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病（20[redacted] 年[redacted]月[redacted] 日～）の2[redacted] 歳男性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第II相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

20[redacted] 年[redacted] 月[redacted] 日の 16 時 1 分，visit 2/week 0 の治験薬の投与が開始された。20[redacted] 年[redacted]月[redacted] 日，visit 4/week 0 が行われた。

投与 51 日後日，被験者は重度の咳嗽，痰，全身性関節痛及び呼吸困難（肺炎と診断され，投与 52 日後に入院を要した）を訴えた。同日，胸部 X 線検査が行われた結果，右心傍肺炎性間質性肺浸潤が認められた。血液検査の結果，クラミジア肺炎が陽性であった。胸部のコンピュータ断層撮影（CT）スキャンの結果，ウイルス性肺炎性間質性肺浸潤又はニューモシスチス肺炎（PCP）が認められた。肺機能検査の結果，重度の気道閉塞疾患及び努力肺活量（FVC）の増加が認められた。被験者は，3 L の酸素（O2）吸入（投与 52 日後の 5 時 0 分から投与 54 日後の 10 時 0 分まで）を受け，抗生物質 Rukasyn/アンピシリン及びジスロマック，コルチコステロイド Solondon(Methysol），並びにホルモテロール投与と共に，呼吸器官の弛緩薬 Avento 吸入／イプラトロピウムによる治療（投与 52 日後から投与 58 日後まで）を受けた。被験者は，タミフルの経口投与，コデインリン酸塩及びタイレノール ER の投与を受けた。投与 58 日後，肺機能検査が再度行われた結果，わずかに気道閉塞疾患が認められ，末梢気道は正常であったが努力呼気流量（FEF）は 25～35%に低下した。投与 58 日後の 12 時 0 分，被験者は肺炎から回復し，同日，退院した。

治験薬の投与は継続された。投与 63 日後，治験責任医師の診察後，治験薬の投与が再開された。

併用薬は，クローン病に対する葉酸，Purinetone，メチロン及び Aronamin C plus であった。被験者に合併症はなかった。

治験責任医師は，治験薬と肺炎との因果関係は「関連なし」と考える。関連する可能性が低い／可能性がないと治験責任医師は判断する。

規制当局への報告目的で，ベーリンガーインゲルハイムは，肺炎と治験薬との因果関係に「合理的な可能性がない」と評価した。

投与 407 日後，本治験の中間非盲検化が行われた。

被験者番号 (Site)

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			

Treatment Group	Age at Study Start	Sex	Race
P1:RISA 600 MG IV / P2:RISA 600 MG IV	3	MALE	ASIAN

Medical History	Onset Year
ANEMIA	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	20

Prior Procedures	Procedure Year
BIOPSY	20
ENDOSCOPY	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	600 mg	IV	Every 4 Weeks	20 / 1	20 / 58	58
Risankizumab	600 mg	IV	Every 4 Weeks	20 / 100	20 / 156	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	250 mg	ONCE	Y-M: 20 -
INFLIXIMAB	260 mg	ONCE	Y-M: 20 -
INFLIXIMAB	260 mg	EVERY 8 WEEKS	Y-M: 20 -
INFLIXIMAB	300 mg	ONCE	Y-M: 20 -
ADALIMUMAB	160 mg	ONCE	Y-M: 20 - / -277
ADALIMUMAB	80 mg	ONCE	Y-M: 20 - / -263

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
FERROUS SULFATE	Not reported.	Not reported.	Not reported.	Not reported.
FOLIC ACID	Not reported.	Not reported.	Not reported.	Not reported.
MESALAZINE	4000 mg	Not reported.	Not reported.	Not reported.
CEFRADINE	Not reported.	Not reported.	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
GRANDPAZE F	Not reported.	Not reported.	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
KETOROLAC TROMETHAMINE	Not reported.	Not reported.	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
NIFEDIPINE	Not reported.	Not reported.	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
TRAMADOL HYDROCHLORIDE	Not reported.	Not reported.	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
GENTAMICIN	Not reported.	Not reported.	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 64
MELILOTUS OFFICINALIS EXTRACT	Not reported.	Not reported.	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 64
ACECLOFENAC	Not reported.	Not reported.	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 64
PARACETAMOL	Not reported.	Not reported.	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 65
VARIDASE	Not reported.	Not reported.	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 65
ANUSOL PLUS	Not reported.	Not reported.	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 67
AMOXICILLIN	Not reported.	Not reported.	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 68

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

Event Description	ANAL ABSCESS
Preferred term	肛門膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 62
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	64
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

20[redacted] 年[redacted]月[redacted] 日に入手した[redacted]からの報告（参照番号：[redacted]）。

韓国の実施医療機関番号[redacted] の治験責任医師から，被験者番号[redacted]に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病の 3[redacted] 歳男性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第 II 相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

20[redacted] 年[redacted] 月[redacted]日，被験者は本治験に登録され，20[redacted] 年[redacted] 月[redacted]日の 16 時 25 分，治験薬の投与が行われた。

投与 58 日後，被験者は事象の発現前に治験薬の最終投与を受けた。投与 60 日後，関連する臨床検査の結果，ヘモグロビンが 10.8（低値），ヘマトクリットが 35.0（低値），リンパ球数が 23.9，好中球数が 63.9，血沈検査（ESR）が 29，血中クレアチニンが 1.0，血中尿素窒素（BUN）が 9，血中クロールが 104，心電図は正常範囲内（WNL），血小板数が 332，赤血球数が 4.75，C-反応性蛋白（CRP）が 3.13 であった。投与 62 日後，直腸鏡検査の結果，複数箇所に馬蹄型膿瘍の再燃が認められた。膿瘍の原発口が確認可能であり，ドレインは使用されていなかった。投与 62 日後，肛門の超音波検査が行われ，結果は不明であった。投与 62 日後，被験者は，同日に入院を要したため重篤と判断された肛門膿瘍を発現した。肛門膿瘍に対して切開及びドレナージ（I&D）による治療が行われた。投与 64 日後，病院で瘻孔切除術及びポリープ（非乾酪性肉芽腫）除去が行われたと電話報告があった。被験者は，感染症に対して投与 62 日後にセフラジン 2 g の静脈内（IV）投与，投与 64 日後から投与 68 日後まで Gomcillin 1500 mg の経口投与，及び投与 62 日後から投与 64 日後までゲンタマイシン 160 mg の筋肉内（IM）投与を受け，疼痛に対して投与 62 日後に Kerola 30 mg の IM 投与，投与 64 日後から投与 65 日後まで Suspen 徐放（ER）1950 mg の PO 投与及び投与 62 日後に Doranzin 50 mg の IM 投与を受け，炎症に対して投与 64 日後に Agafen 300 mg の PO 投与，投与 65 日後から投与 68 日後まで Talniflumate 1100 mg

の PO 投与，投与 65 日後に Inpra 2.2 ml の IM 投与を受け，抗炎症薬として投与 64 日後から投与 65 日後まで Versed 30 mg の PO 投与の受け，痔瘻の緩和目的の投与 64 日後から投与 67 日後まで Hemorex 坐剤 40 mg/直腸（PRE）投与，疼痛増悪に対して投与 65 日後から 2 投与 68 日後まで Ketoracin 20 mg の PO 投与を受け，術後（OP）感染症に対して投与 65 日後から投与 68 日後まで Neonase 30 mg の PO 投与を受けた。投与 64 日後，被験者は肛門膿瘍から回復し，同日，退院した。

治験薬の投与は継続された。

併用薬は，クローン病（20[redacted]年[redacted]月[redacted]日に発症）に対するメサラジン，貧血（20[redacted]年[redacted]月[redacted]日に発症）に対する Feroba-U 及び葉酸，機能性腸疾患に対する Pentacol，高血圧予防目的の Adalat，痔に対する Nesbiron 及び Venitol であった。その他の合併症は，下痢及び腹痛（いずれも 20[redacted]年[redacted]月～）であった。前治療として，5-アミノサリチル酸（5-ASA），コルチコステロイド，アザチオプリン，メトトレキサート，鉄剤，葉酸，レミケード，ヒュミラ，ベドリズマブ，及びトファシチニブの投与歴があった（使用理由不明）。被験者の病歴は報告されなかった。

治験責任医師は，治験薬と肛門膿瘍との因果関係は「関連なし」と考える。しかし，治験責任医師から痔瘻及び膿瘍と治験薬との因果関係評価は報告されていないとのことだった。

規制当局への報告目的で，ベーリンガーインゲルハイムは，肛門膿瘍と治験薬との因果関係に「合理的な可能性がない」と評価した。

投与 583 日後，本治験の中間非盲検化が行われた。

被験者番号[redacted] (Site[redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
腹部膿瘍	X	X		X
肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ABOMINAL PAIN	Not reported.
ANEMIA	Not reported.
DIARRHEA	Not reported.
IDIOPATHIC OSTEOPOROSIS	Not reported.
INTERMITTANT MILD FEVER	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	20[redacted]

Prior Procedures	Procedure Year
BIOPSY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	250 mg	ONCE	Y-M: 20[redacted]
INFLIXIMAB	265 mg	ONCE	Y-M: 20[redacted]
INFLIXIMAB	270 mg	EVERY 8 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	300 mg	EVERY 8 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	250 mg	EVERY 8 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	300 mg	ONCE	Y-M: 20[redacted]

ADALIMUMAB	80 mg	ONCE	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 4 WEEKS	Y-M: 20[redacted]
FOSAVANCE	Not reported.	Not reported.	Y-M: 20[redacted] / -15

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOSAVANCE	Not reported.	Not reported.	Y-M: 20[redacted] / -15	Not reported.
MORPHINE HYDROCHLORIDE	Not reported.	Not reported.	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 22
PETHIDINE	Not reported.	Not reported.	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 22
PETHIDINE	Not reported.	Not reported.	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 33
CEFTRIAXONE SODIUM	Not reported.	Not reported.	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 36
METRONIDAZOLE	Not reported.	Not reported.	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 36
RANITIDINE	Not reported.	Not reported.	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 24
VITAMINS NOS	Not reported.	Not reported.	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 32
METOCLOPRAMIDE	Not reported.	Not reported.	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 31
LIDOCAINE	Not reported.	Not reported.	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 32
PANTOPRAZOLE	Not reported.	Not reported.	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 32
CHLORHEXIDINE	Not reported.	Not reported.	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 38
FAMOTIDINE	Not reported.	Not reported.	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 40
AMBROXOL	Not reported.	Not reported.	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 44
PETHIDINE	Not reported.	Not reported.	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 47
ALBUMIN HUMAN	Not reported.	Not reported.	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
FENTANYL	Not reported.	Not reported.	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
FUROSEMIDE	Not reported.	Not reported.	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
GLYCOPYRRONIUM BROMIDE	Not reported.	Not reported.	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34

GRANISETRON	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 34 34
HYDROMORPHONE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 34 34
LIDOCAINE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 34 34
PROPOFOL	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 34 34
PYRIDOSTIGMINE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 34 34
REMIFENTANIL	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 34 34
ROCURONIUM BROMIDE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 34 34
VECURONIUM BROMIDE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 34 34
ALBUMIN HUMAN	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 35 35
CHLORPHENAMINE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 35 35
VITAMINS NOS	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 35 36
AMBROXOL	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 35 40
METOCLOPRAMIDE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 36 38
PIPERACILLIN W/TAZOBACTAM	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 36 46
ALBUMIN HUMAN	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 37 40
LEVOFLOXACIN	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 39 40
ACETYLCYSTEINE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 39 43
VITAMINS NOS	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 40 40
PARACETAMOL	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 41 41
OXYCODONE HYDROCHLORIDE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 41 45
BESZYME	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 41 61
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 41 61
TARGIN	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 41 72
AMBROXOL	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 42 43

CODENA-S	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 42 / 54
KETOPROFEN	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 45 / 45
MOXIFLOXACIN	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 47 / 53

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

Event Description	ABDOMINAL ABSCESS
Preferred term	腹部膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 23 (22 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	47 (46 DAYS AFTER LAST TREATMENT)
Duration of AE	25 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	HAP (HOSPITAL ACQUIRED PNEUMONIA)
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 36 (35 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	46 (45 DAYS AFTER LAST TREATMENT)
Duration of AE	11 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED

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

Generated: [redacted] 20[redacted]:12:37
Program Source Code: [redacted]

20[redacted] 年[redacted] 月[redacted] 日に入手した[redacted]からの報告（参照番号：[redacted]）。

**注：BI 655066 は ABBV-066（リサンキズマブ）と同義とする。

韓国の実施医療機関番号[redacted] の治験責任医師から，被験者番号[redacted] に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病の 2[redacted] 歳男性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第 II 相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

20[redacted] 年[redacted] 月[redacted] 日，被験者は本治験に登録された。20[redacted] 年[redacted]月[redacted] 日，治験薬の投与が開始され，これは被験者が本事象発現前に受けた治験薬の最終投与であった。

投与 16 日後，被験者は，腹部膿瘍の症状である中等度の腹痛増悪を発現した。投与 22 日後，被験者は外来病棟（OPD）を受診し，報告から 1 週間前に始まった腹痛の進行を訴えた。医師は，被験者の右下腹部（RLQ）を評価し，腹部膿瘍と診断した。被験者は，腹部のコンピュータ断層撮影（CT）スキャンのため救急治療室（ER）を受診した。CT スキャンの結果，4.5 cm 大のガスを含んだ新たな腹部膿瘍が認められた。同日，被験者は，腹部膿瘍の経皮的ドレナージを受けた。複雑な液貯留のため，8.5 Fr の経皮ドレナージ用カテーテル（PCD）が腹部中央（臍孔のすぐ下）に挿入された。投与 22 日後，腹部及び骨盤部の CT スキャンの結果，回腸内及び結腸全体に肉眼的に変化がないクローン病の関与が認められ，腹腔内上部の正中線に 5.4 cm 大のガスを含んだ大網膿瘍が新たに認められた。同日，臨床検査の結果は，ヘモグロビンが 9.9，リンパ球数が 13.5 及び血小板数が 571000 であった。投与 22 日後，腹痛増悪に対してセフトリアキソン sod，メトロニダゾール及びモルヒネ塩酸塩（HCl）の投与が開始された。同日，PCD 挿入の前投薬としてペチジンも投与され，投与 23 日後に再度投与され，投与 33 日後に増量して投与された。

投与 23 日後，被験者は，同日に入院を要した腹部膿瘍と診断された。投与開始月に腹痛増悪が初めて認められていたが，治験責任医師は，腹部膿瘍及び入院は同日に判断されている事実

に基づいて発現日を判断した。入院時，被験者は結腸瘻の疼痛も訴え，セフトリアキソ及びメトロニダゾールによる治療が行われた。被験者の腹部に PCD が再度挿入され，被験者は抗生物質の静脈内（IV）投与を受けた。絶食（NPO）は継続された。

投与 26 日後（入院中），被験者は非経口ボリューム補助及び抗生物質の IV 投与による治療を受けた。被験者の症状はその後数日間改善せず，継続された非外科的療法は疾患進行増悪を改善しないように思われた。

投与 30 日後，瘻孔造影検査の結果，膿瘍腔と近傍横行結腸の間に瘻管が 2 つ認められた。管外腔への造影剤漏出の疑いも見つかった。被験者の術前の診断は，大網膿瘍及び結腸瘻であった。投与 34 日後，被験者は結腸亜全摘除（クローン病に起因する T 結腸瘻を伴う腹腔内膿瘍）及び虫垂切除を受けた。

投与 33 日後，治験薬の投与は中止された。

投与 35 日後，血液検査の結果は，白血球（WBC）が 13770 又は 13.77 uL，赤血球（RBC）が 3.25x100^3/uL，ヘモグロビンが 7.7 g/dL，ヘマトクリットが 25.7%，血小板が 285K，好中球分葉核球（seg.）が 88.8，リンパ球が 4.0，総蛋白が 5.5，アルブミンが 2.5，C-反応性蛋白（CRP）が 0.42 及びプロラクチンが 2.42 であった。被験者は赤血球（RBC）減少に対して輸血を受けていた。輸血後の投与 36 日後，血液検査の結果は，RBC（4.30x100^3/uL），血中ヘモグロビン（10.6 g/dL）及び血中ヘマトクリット（34.2%）の上昇であった。

投与 36 日後，被験者は，入院延長のため重篤と判断された HAP（院内肺炎）を発現した。PCD が抜去され，培養が行われた結果，Klebsiella pneumonia ssp pneumonia が認められた。バイタルサインは，血圧が 135/81 mmHg，心拍数が 142 bpm，体温が 38.7°C，呼吸数が 20 回／分であった。胸部の前後像（AP）から，肺炎の可能性が高かった。追加の臨床検査の結果は，WBC が 28250 uL，血小板が 247K，好中球分葉核球が 88.3 及び 92.6%，リンパ球が 4.5 及び 1.7%，総蛋白が 5.9，アルブミンが 3.2，並びに CRP が 1.56 及び 3.58 mg/dL であった。NPO が継続され，Tazocin 及びレボフロキサシンが抗生物質の静脈内投与として追加された。

投与 37 日後，臨床検査の結果は，WBC 数が 36.47，RBC 数が 3.85，ヘモグロビンが 9.7，ヘマトクリットが 30.7，血小板が 243K，好中球分葉核球が 93，リンパ球が 3，総蛋白が 5.2，アルブミンが 2.7 及び CRP が 6.53 であった。投与 38 日後，発熱及び頻脈などの感染症症状が持続していたが，末梢静脈挿入式中心静脈カテーテル（PICC）は抜去された。投与 39 日後，臨床検査の結果は，WBC 数が 14.10，RBC 数が 2.92，ヘモグロビンが 7.5，ヘマトクリットが 23.6，血小板が 211K，好中球分葉核球が 81.1，リンパ球が 5.6，総蛋白が 4.6，アルブミンが 2.5 及び CRP が 10.05 であった。投与 40 日後，臨床検査の結果は，WBC 数が 6.87，RBC 数が 2.90，ヘモグロ

ビンが 7.1，ヘマトクリットが 23.6，血小板が 202K，好中球分葉核球が 74.3，リンパ球が 10.5，総蛋白が 4.7，アルブミンが 2.6 及び CRP が 6.75 であった。胸部の PA 検査の結果から，気管支肺炎の可能性が高かった。食事の経口摂取及び薬剤の経口投与が再開された日の同日，IV 療法が中止された。

投与 41 日後，GMS 染色検査が行われた結果，結腸の組織構造が明らかとなった。結腸亜全摘除で摘出された慢性活動性炎症を含む組織から，飛び石病変，貫壁性炎症，多発性非乾酪性肉芽腫及び網に広がる膿瘍形成がさらに認められ，これらは全てクローン病と一致していた。肉芽腫を伴う反応性リンパ節（63）も認められた。検査の結果，虫垂の組織構造も明らかとなり，虫垂切除に膿瘍を伴う貫壁性慢性活動性炎症及び非乾酪性肉芽腫が含まれており，クローン病関与と一致していた。

投与 42 日後，臨床検査の結果は，WBC 数が 4.51，RBC 数が 3.98，ヘモグロビンが 10.2，ヘマトクリットが 33.4，血小板が 282K，好中球分葉核球が 62.6，リンパ球が 15.3，総蛋白が 5.4，アルブミンが 3.1 及び CRP が 3.63 であった。投与 44 日後，臨床検査の結果は，WBC 数が 4.06，RBC 数が 3.94，ヘモグロビンが 10.0，ヘマトクリットが 33.2，血小板が 343K，好中球分葉核球が 63.5，リンパ球が 15.9，総蛋白が 5.7，アルブミンが 3.2 及び CRP が 1.31 であった。同日，胸部の PA 検査が行われ，肺炎の改善が認められた。投与 46 日後，臨床検査の結果は，WBC 数が 4.52，RBC 数が 4.06，ヘモグロビンが 10.7，ヘマトクリットが 33.4，血小板が 338K，好中球分葉核球が 56.0，リンパ球が 21.2，総蛋白が 6.2，アルブミンが 3.4 及び CRP が 0.7 であった。投与 46 日後，被験者は HAP（院内肺炎）から回復した。投与 47 日後，被験者は腹部膿瘍及び瘻孔から回復し，同日，安定し改善しており，中等度の身体活動及び経口摂取に耐えうる状態で退院した。退院時に処方された薬剤には抗生物質が含まれていた。

投与 83 日後，被験者は，非重篤と判断されたグレード 1 の腹部不快感を発現した。腹部不快感に対する治療が行われた（詳細不明）。被験者は腹部不快感から回復していなかった。

併用薬は，特発性骨粗鬆症（20[redacted]年[redacted]月[redacted]日に発症）に対する Fosamax plus D，メトクロプラミド，パントプラゾール，グラニセトロン，ファモチジン，リドカインパッチ 2%，アンブロキソール，クロルヘキシジン，フェンタニル，フロセミド，レミフェンタニル，ヒドロモルフォン，ピリドスチグミン，Glycopyrrolate，プロポフォール，クロルフェニラミン，Tarzoferan，レボフロキサシン，アセチルシステイン，Beszyme，Targin，オキシコドン塩酸塩水和物，アセトアミノフェン，Motilitone，モキシフロキサシン，ラニチジン及び咳止めシロップ（これらは全て使用理由不明），腹痛増悪に対するセフトリアキソンナトリウム（sod），メトロニダゾール及びモルヒネ塩酸塩（HCL），PCD 挿入の前投薬としてペチジンであった。その他の合併症は，腹痛及び下痢（いずれも 20[redacted]年[redacted]月～），軽度の間欠性発熱（20[redacted]年[redacted]月[redacted]日～）及び貧血（20[redacted]年[redacted]月[redacted]日～）であった。

前治療として，5-アミノサリチル酸（5-ASA），ベクロメタゾン，コルチコステロイド，アザチオプリン，メトトレキサート，レミケード，ヒュミラ及びベドリズマブの投与歴があった（使用理由不明）。既往歴は，瘻孔切除術，並びに切開及びドレナージ（I & D）であった。

治験責任医師は，治験薬と腹部膿瘍，HAP（院内肺炎）及び腹部不快感との因果関係は「関連なし」と考える。

規制当局への報告目的で，ベーリンガーインゲルハイムは，腹部膿瘍，HAP（院内肺炎）及び腹部不快感と治験薬との因果関係に「合理的な可能性がない」と評価した。

投与 419 日後，本治験の中間非盲検化が行われた。

Causality for ABBV-066 (Blinded)

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1) Event of ABDOMINAL ABSCESS

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

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

2) Event of SEVERE HAP (HOSPITAL ACQUIRED PNEUMONIA)

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

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

3) Event of ABDOMINAL DISCOMFORT (non-serious)

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

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

Alternative Etiology for ABBV-066 (Blinded)

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1) Event of ABDOMINAL ABSCESS

AbbVie: More likely related to the history of crohn's disease and its complications.

2) Event of SEVERE HAP (HOSPITAL ACQUIRED PNEUMONIA)

AbbVie: More likely related to the history of hospitalization and its complications, the event occurred one month post study drug.

3) Event of ABDOMINAL DISCOMFORT (non-serious)

AbbVie: More likely related to the history of crohn's disease and its complications.

被験者番号[redacted] (Site[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			
アフタ性潰瘍	X			
無力症	X			

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

Medical History	Onset Year
ANEMIA	Not reported.
APHTHOUS STOMATITIS	Not reported.
ARTHRALGIA	Not reported.
GLUCOCORTICOID INDUCED OSTEOPOROSIS	Not reported.
LOW BACK PAIN	Not reported.
SERONEGATIVE RHEUMATOID ARTHRITIS	Not reported.
PRIMARY DIAGNOSIS: CROHN"S DISEASE	20[redacted]

Prior Procedures	Procedure Year
BIOPSY	20[redacted]
ENDOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
TOBACCO	FORMER	Not reported.	Not reported.	Not reported.

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Not reported.

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 100	[redacted]20[redacted] / 127	28

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	Not reported.	Not reported.	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	ONCE	Y-M: 20[redacted]
INFLIXIMAB	10 mg/kg	ONCE	Y-M: 20[redacted]

INFLIXIMAB	10 mg/kg	ONCE	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	EVERY 8 WEEKS	Y-M: 20[redacted]
BENZYDAMINE	Not reported.	Not reported.	Y-M: 20[redacted] / -355
INFLIXIMAB	10 mg/kg	EVERY 8 WEEKS	Y-M: 20[redacted] / -131

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CALCIUM CITRATE W/COLECALCIFEROL	Not reported.	Not reported.	Not reported.	Not reported.
FOLIC ACID	Not reported.	Not reported.	Not reported.	Not reported.
FOSAVANCE	Not reported.	Not reported.	Not reported.	Not reported.
HYDROXYCHLOROQUINE	Not reported.	Not reported.	Not reported.	Y-M: 20[redacted] / 9
PREDNISOLONE	Not reported.	Not reported.	Not reported.	Y-M: 20[redacted] / 9
POTASSIUM CHLORIDE	Not reported.	Not reported.	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 14
VITAMINS NOS	Not reported.	Not reported.	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 25
LORAZEPAM	Not reported.	Not reported.	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 11
MORPHINE HYDROCHLORIDE	5 mg	Not reported.	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 12
MORPHINE HYDROCHLORIDE	Not reported.	Not reported.	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 12
TRIAMCINOLONE ACETONIDE	Not reported.	Not reported.	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 15
ZINC SULFATE	Not reported.	Not reported.	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 24
PROPACETAMOL	Not reported.	Not reported.	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 12
PIPERACILLIN W/TAZOBACTAM	Not reported.	Not reported.	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 22
ALBUMIN HUMAN	Not reported.	Not reported.	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
RED BLOOD CELLS, CONCENTRATED	Not reported.	Not reported.	Y-M: 20[redacted] / 18	Y-M: 20[redacted] / 18
MORPHINE HYDROCHLORIDE	5 mg	Not reported.	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21
HEPARIN	Not reported.	Not reported.	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
VITAMINS NOS	Not reported.	Not reported.	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 69

POTASSIUM CHLORIDE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 65 65
CEFTRIAXONE SODIUM	2000 mg	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 65 69
DEXAMETHASONE	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 65 69
METRONIDAZOLE	1500 mg	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 65 69
MORPHINE HYDROCHLORIDE	10 mg	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 67 69
POSELAMIN	Not reported.	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 68 68
CEFIXIME	400 mg	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 69 75
METRONIDAZOLE	1000 mg	Not reported.	Y-M: 20[redacted] / Y-M: 20[redacted] / 69 75

Event #1: Serious Adverse Event

Event Description	SEVERE APHTHOUS STOMATITIS
Preferred term	アフタ性潰瘍
AE Onset Date / Rx Day	[redacted]20[redacted]:14:56 / 10
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	26
Duration of AE	17 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	ANEMIA AGGRAVATED
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 15
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	

SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	22
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	WORSENING OF GENERAL WEAKNESS
Preferred term	無力症
AE Onset Date / Rx Day	[redacted]20[redacted] / 64
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	69
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:12:37
Program Source Code: [redacted]

20[redacted] 年[redacted] 月[redacted] 日に入手した[redacted]からの報告（参照番号：[redacted]）。

注：BI 19185 は ABBV-066（リサンキズマブ）と同義とする。

韓国の実施医療機関番号[redacted] の治験責任医師から，被験者番号[redacted] に関する情報を入手した。本被験者は，中等度から重度の活動性クローン病の 4[redacted]歳男性患者であり，抗 TNF 療法の投与歴がない又は前治療歴のある中等度から重度の活動性クローン病患者に対して，IL-23 p19 拮

抗モノクローナル抗体である BI 655066 の有効性，薬物動態及び安全性を評価する第 II 相，多施設共同，無作為化，二重盲検，反復投与，プラセボ対照，並行群間試験である 1311.6 試験に登録された。

被験者は濃厚赤血球（RBC）輸血を受けた。輸血後の 20[redacted] 年[redacted] 月，以下の臨床検査結果を入手した（RBC 3.53 x 1003 µL，ヘモグロビン 9.3 g/dL 及びヘマトクリット 29.5%）。

20[redacted] 年[redacted] 月[redacted] 日，被験者は治験に登録され，20[redacted] 年[redacted] 月[redacted] 日の 13 時 25 分，治験薬の投与が開始された。

投与 10 日後，被験者は，入院を要した重度のアフタ性口内炎を発現した。被験者は，口腔内にグレード 2 のアフタ性口内炎（投与 3 日後～）を発現した。アフタ性口内炎は，リウマチ治療薬のメトトレキサート，プレドニゾロン，ヒドロキシクロロキン（MTX，PD，HCQ）の副作用に起因するため重篤と判断された。悪化がひどく，被験者は何も食べることができなかった。同日，被験者は，補助的治療のため入院した。被験者は，栄養障害を示す口腔潰瘍があった。治験責任医師は，アフタ性口内炎は本被験者のベースライン症状であり，重篤な有害医事象（SAE）基準を満たした日の同日に増悪したことを確認した。投与 11 日後，被験者の左腕に末梢静脈挿入式中心静脈カテーテル（PICC）が留置され，被験者は絶食（NPO）となった。非経口高カロリー栄養補助及び抗生物質セフトリアキソンナトリウム及びメトロニダゾールの静脈内（IV）投与による治療が行われた。投与 12 日後，抗生物質の IV 投与は Tasoferan に変更された。臨床検査の結果は，C-反応性蛋白（CRP）が 10.53 mg/dL，白血球（WBC）が 17040 µL，好中球絶対数（ANC）が 12.558 x 10^3 µL であり，被験者の体温は 40°C であった。

投与 15 日後，被験者は，入院を延長した貧血増悪を発現した。同日，被験者は眼科・耳鼻咽喉科医（ENT OPD）の診察を受け，潰瘍部位に Oramedy 軟膏（oint）を塗るように指導され，被験者は経口摂取を再開した。

投与 18 日後，臨床検査の結果は，白血球（WBC）が 7400 µL，赤血球（RBC）が 2.69 x 1003 µL，ヘモグロビンが 7.2 g/dL 及びヘマトクリットが 22.7%であった。

投与 22 日後，**被験者は貧血増悪から回復した。同日，抗生物質の静脈内投与は中止された。臨床検査の結果は，**C-反応性蛋白（CRP）が 0.53 mg/dL，白血球（WBC）が 9200 µL，好中球分葉核球が 49.4%及び好中球絶対数（ANC）が 4.54 x 10^3/µL であった。

投与 26 日後，被験者は重度のアフタ性口内炎から回復し，退院した。同日，被験者の非左腕に挿入されていた PICC が抜去された。被験者は 7～8 kg の体重増加があった。次回の治療は投与 29 日後を予定されていた。

投与から約 2 か月後，被験者は，入院のため重篤と判断された全身性脱力悪化（1 回目）を発現した。全身性脱力悪化に対して治療が行われた（詳細不明）。

治験責任医師は，重度のアフタ性口内炎は 1 度のみ発現しており，2 回目の発現はなかったことを指摘した。同じ事象が報告されていたが，誤報であった。本事象報告時点での重篤な有害事象は全身性脱力悪化であり，重度のアフタ性口内炎ではなかった。

投与 64 日後，被験者は，入院を要したため重篤と判断されグレード 2 の全身性脱力悪化（2 回目）を発現した。被験者は，全身性脱力悪化（投与 64 日後～）に起因する口内炎，口腔内痛及び体重減少（15 日間で 4 kg）を訴えた。同日，被検者は補助的治療のため入院した。血液検査及び胸部 X 線検査が行われた。投与 64 日後，被験者は，ビタミン欠乏に対して Tamipool 1 バイアルの静脈内（IV）投与を受けた。投与 65 日後，ENT OPD の診察が行われ，潰瘍部位に噴霧する Neo Mucosal Activator スプレー10 g 1 日 3 回及び食事前の Dexa solution（sol）100 mL 1 日 3 回のうがい薬がアフタ性口内炎に対して処方された。被験者の臨床検査の結果は，CRP が 7.52 mg/dL，WBC が 14900 uL，好中球分葉核球が 57.6%，血小板が 514K 及び ANC が 8.58 x 10 ^3/uL であった。投与 65 日後，アフタ性口内炎の治療として Oramedy（R）10 g 軟膏及びベンジダミンうがい薬 100 mL の使用が開始された。疼痛緩和目的及びクローン病に対するモルヒネ塩酸塩（HCl）5 mg の IV 投与，並びに低カリウム血症に対する塩化カリウム（KCL）600 mg 1 日用量 2400 mg の経口投与（いずれも投与 65 日後に開始）が行われた。投与 67 日後，被験者はクローン病に対してモルヒネ塩酸塩（HCl）5 mg 1 日 2 回の IV 投与による治療を受けた。

投与 68 日後，被験者は仙腸関節（SI）及び尾骨部位の疼痛があった。骨盤骨の X 線検査の結果，全身性の骨密度低下が認められ，その他の骨異常は認められなかった。被験者はモルヒネ 10 mg の IV 投与を受け，関節痛が緩和された。栄養不均衡に対して Potenamin 500 mL の IV 投与が行われた。

被験者は全身性脱力（1 回目）から回復していなかった。投与 69 日後，被験者は全身性脱力（2 回目）から回復し，退院した。被験者の状態は安定しており，改善が認められ，被験者は 5 日間で 3 kg の体重増加があった。Tamipool，Dexa，Neo Mucosal Activator スプレー，セフトリアキソンナトリウム，メトロニダゾール及びモルヒネ塩酸塩（HCl）の投与が中止された。同日，クローン病に対してセフィキシム 200 mg 及びメトロニダゾール 500 mg（いずれも 1 日 2 回の経口投与）が開始され，投与 75 日後に中止された。次回の治療は投与 92 日後を予定されていた。

これら事象の発現後，治験薬の投与は継続された。

併用薬は，貧血（20[redacted] 年[redacted] 月～）に対する葉酸，グルココルチコイド誘因性骨粗鬆症（20[redacted] 年[redacted]月[redacted] 日～）に対する Fosamax plus D 及び Calteo 40 R，クローン病に対するセフトリアキソン SOD 及びメトロニダゾールであった。その他の合併症は，血清反応陰性関節リウマチ（20[redacted] 年～），アフタ性口内炎（20[redacted] 年[redacted] 月～），関節痛（20[redacted] 年[redacted] 月～），腰痛（20[redacted] 年[redacted] 月～）下痢，腹痛，全身性脱力（20[redacted] 年[redacted]月[redacted] 日～），経口摂取不良，体重減少，ビタミン欠乏，低カリウム血症及び栄養不均衡であった。

前治療として，関節リウマチ（血清反応陰性）に対するプレドニゾロン，ヒドロキシクロロキン及びメトトレキサート，並びにコルチコステロイド，ベクロメタゾン，アザチオプリン，メトトレキサート，レミケード，ヒュミラ及び Remsima（使用理由不明）の投与歴があった。手術歴は及び既往歴は報告されなかった。

治験責任医師は，治験薬と重度のアフタ性口内炎，貧血増悪及び全身性脱力悪化（全 2 回分）との因果関係は「関連なし」と考える。

規制当局への報告目的で，ベーリンガーインゲルハイムは，重度のアフタ性口内炎，全身性脱力悪化（1 回目及び 2 回目），並びに貧血増悪と治験薬との因果関係に「合理的な可能性がない」と評価した。

投与 296 日後，本治験の中間非盲検化が行われた。

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1) SEVERE APHTHOUS STOMATITIS

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

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

Alternative Etiology for ABBV-066 (open label)

Event of SEVERE APHTHOUS STOMATITIS

AbbVie: More likely related to pre-existing aphthous stomatitis associated to marasmus/malnutrition, complication of underlying crohn's disease, use of Methotrexate, Prednisolone, Hydroxychloroquine

2) WORSENING GENERAL WEAKNESS

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

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

Alternative Etiology for ABBV-066 (Open label)

Event of WORSENING GENERAL WEAKNESS

AbbVie: More likely related to natural course of pre-existing condition associated to complications of underlying crohn's disease and rheumatoid arthritis and their comorbidities

3) ANEMIA AGGRAVATED

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

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

Alternative Etiology for ABBV-066 (Open label)

Event of ANEMIA AGGRAVATED

AbbVie: More likely related to complication of pre-existing crohn's disease and rheumatoid arthritis

4) WORSENING OF GENERAL WEAKNESS

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

Causality as per Mfr. (Drug/Vaccine):

Alternative Etiology for ABBV-066 (Open label)

Event of WORSENING OF GENERAL WEAKNESS

AbbVie: More likely related to natural course of pre-existing condition associated to complications of underlying crohn's disease and rheumatoid arthritis and their comorbidities

M16-006 試験

治験の標題： A Multicenter, Randomized, Double-Blind, Placebo Controlled Induction Study of the Efficacy and Safety of Risankizumab in Subjects with Moderately to Severely Active Crohn's Disease
施設数 / 実施国名： 297 施設 / 39 ヵ国（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，ブラジル，ブルガリア，カナダ，チリ，中国，クロアチア，チェコ共和国，エストニア，ドイツ，ギリシャ，イスラエル，イタリア，日本，ラトビア，マレーシア，メキシコ，オランダ，ニュージーランド，ノルウェー，ポーランド，ポルトガル，ルーマニア，ロシア，セルビア，シンガポール，スロバキア，南アフリカ，韓国，スペイン，スウェーデン，スイス，ウクライナ，イギリス，米国）
治験責任医師： [redacted], PhD，他
公表文献 (参考資料) ： なし
治験期間： 最初の被験者の初回来院日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日 開発のフェーズ：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： 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：855 例 解析時：931 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 85 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。生物学的製剤による前治療で効果不十分又は不耐容であった被験者（以下「Bio-IR」）及び生物学的製剤以外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「non 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 又はリサンキズマブ 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，及び臨床検査値を評価した。

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［0，1，1 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［0，1，1 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：
安全性解析は，治験薬を 1 回以上投与されたすべての被験者を含む安全性解析対象集団を用いて実施した。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，臨床検査値，及び製品品質苦情を解析した。

内訳

12 週導入療法期では，931 例（リサンキズマブ 600 mg IV 群 373 例，1200 mg IV 群 372 例，プラセボ群 186 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 97.9%，1200 mg IV 群 98.4%，プラセボ群 87.6%）。

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。278 例が組み入れられ，リサンキズマブ 180 mg SC 群 67 例，360 mg SC 群 68 例，1200 mg IV 群 67 例がランダム化され，76 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 95.3%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 43.5%，臨床的 CDAI 寛解 45.2%，以下同順）及び 1200 mg IV 群（41.0%，41.6%）でプラセボ群（21.7%，24.6%）と比較して統計学的に有意に高かった（$P < 0.001$）。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（40.3%）及び 1200 mg IV 群（32.1%）でプラセボ群（12.0%）と比較して統計学的に有意に高かった（$P < 0.001$）。Co-primary endpoints はいずれも，主要な部分集団である non Bio-IR 部分集団及び Bio-IR 部分集団で明確な効果が示され，non Bio-IR 部分集団の方が有効性が高く，エフェクトサイズが大きかった。全体として，全体集団及び部分集団のいずれも，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。

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 86.7%，360 mg SC 群 72.5%，1200 mg IV 群 81.0%，プラセボ / リサンキズマブ 1200 mg IV 群 84.5%）。

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の導入療法を受けた被験者では，intensive PK を含む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 39.4 µg/mL，1200 mg IV では 73.1 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 1.4%（10/736 例），中和抗体が陽性であった被験者は 1 例（0.1%）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 1.1%（3/269 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 1 例であった。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 3.57–4.29 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 10–567 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，リサンキズマブ 600 mg IV 群で 56.3%，1200 mg IV 群で 51.3%であり，プラセボ群で 56.5%と同様であった。重篤な有害事象，高度の有害事象，及び治験薬の投与中止に至った有害事象の発現割合は，リサンキズマブ 600 mg IV 群及び 1200 mg IV 群でプラセボ群と比較して低かった。死亡はリサンキズマブ各群では認められず，プラセボ群で 2 例に認められた。リサンキズマブ 600 mg IV 群及び 1200 mg IV 群で発現割合が高かった有害事象は，頭痛（リサンキズマブ 600 mg IV 群 6.4%，1200 mg IV 群 5.4%，プラセボ群 4.3%，以下同順），上咽頭炎（5.9%，5.9%，2.7%），及び疲労（4.3%，4.0%，3.2%）であった。有害事象のほとんどが軽度又は中等度であった。特に注目すべき事象の発現割合は 5.1%以下であり，発現割合が高かった特に注目すべき事象は過敏症（5.1%，4.3%，3.2%），肝関連事象（2.4%，1.6%，2.2%），及び重篤な感染症（0.8%，0.5%，3.8%）であった。委員会判定された主要心血管イベント（以下「MACE」），委員会判定された Extended MACE，悪性腫瘍，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。活動性結核は，リサンキズマブ 600 mg IV 群の 1 例に 1 件認められた。当該被験者は治験薬を 3 回投与された後に，非重篤な発熱のために治験を中止した。その後，非重篤な活動性肺結核の再燃が報告されたが，本事象は治験責任（分担）医師により治験薬と関連なしと判断された。重篤な感染症の発現割合はプラセボ群で数値的に高く，これは主にプラセボを投与された被験者における原疾患に関連する事象によるものであった。過敏症の有害事象の発現割合は，リサンキズマブ各群とプラセボ群でおおむね同様であった。注射部位反応（注入に伴う反応を含む）の発現割合は，リサンキズマブ各群でわずかに数値的に高く，いずれの事象も軽度又は中等度であった。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。肝関連事象の発現割合は投与群間で同様であり，ほとんどの事象は一過性の肝酵素上昇で，投与の変更はなかった。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。有害事象，臨床検査値，又はバイタルサインに，用量依存的な傾向は認められなかった。新たな安全性のリスクは特定されず，全体として安全性プロファイルは，リサンキズマブの既知の安全性プロファイルと一致していた。

導入療法期 2 では，有害事象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 群で 46.3%，360 mg SC 群で 50.0%，1200 mg IV 群で 52.2%，プラセボ / リサンキズマブ 1200 mg IV 群で 52.6%であった。全体で，重篤な有害事象の発現割合は 5.0%以下であり，高度の有害事象の発現割合は 5.0%であった。リサンキズマブ 360 mg SC 群の 1 例で，治験薬の投与中止に至った有害事象が認められた。死亡は認められなかった。発現割合が高かった有害事象は，頭痛（リサンキズマブ 180 mg SC 群 1.5%，360 mg SC 群 4.4%，1200 mg IV 群 3.0%，プラセボ / リサンキズマブ 1200 mg IV 群 6.6%，以下同順），関節痛（4.5%，0%，3.0%，3.9%），及

び貧血（0%，2.9%，1.5%，5.3%）であった。有害事象のほとんどが軽度又は中等度であった。特に注目すべき事象の発現割合は過敏症を除いて，6%以下であった。発現割合が高かった特に注目すべき事象は過敏症（4.5%，2.9%，10.4%，7.9%），肝関連事象（0%，0%，6.0%，1.3%），及び注射部位反応（0%，1.5%，4.5%，5.3%）であった。委員会判定された MACE，委員会判定された Extended MACE，活動性結核，日和見感染（結核及び帯状疱疹を除く），悪性腫瘍（非黒色腫皮膚癌［NMSC］を除く），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，軽度又は中等度であり，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。

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。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。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。

SA-ALL 集団（試験期間中にリサンキズマブを 1 回以上投与されたすべての被験者）を用いた安全性解析の結果から，新たな安全性の懸念は認められなかった。

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，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 12 週時の高感度 C 反応性蛋白（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いたが，抗薬物抗体を発現した被験者におけるリサンキズマブの血清中曝露量

は，抗薬物抗体が陰性であった被験者と比較して同様かわずかに低く，リサンキズマブの曝露量に及ぼす中和抗体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
治験薬と関連ありの有害事象	表 7	表 8
高度の有害事象	表 9	表 10
死亡に至った有害事象	表 11	-
重篤な有害事象	表 12	表 13
中止に至った有害事象	表 14	表 15

表1

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RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - CLINICAL/STATISTICAL
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TABLE 14.1__1.20.2

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

Exposure to study drug	Placebo IV (N=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Total (N=931) n (%)
Duration interval (days)				
1 - 28	9 (4.8)	3 (0.8)	3 (0.8)	15 (1.6)
29 - 56	8 (4.3)	3 (0.8)	3 (0.8)	14 (1.5)
57 - 84	122 (65.6)	275 (73.7)	256 (68.8)	653 (70.1)
85 - 112	47 (25.3)	92 (24.7)	110 (29.6)	249 (26.7)
> 112	0	0	0	0
Duration (days)				
n	186	373	372	931
Mean (SD)	79.0 (14.08)	83.0 (7.08)	83.0 (6.78)	82.2 (8.97)
Median	84.0	84.0	84.0	84.0
Min, Max	28, 99	28, 112	28, 99	28, 112

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] 21:06 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.1__2.7

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

	Risankizumab			Placebo IV/ Risankizumab	
Exposure to study drug	180 mg SC (N=67) n (%)	360 mg SC (N=68) n (%)	1200 mg IV (N=67) n (%)	1200 mg IV (N=76) n (%)	Total (N=278) n (%)
Duration interval (days)					
1 - 28	0	0	1 (1.5)	2 (2.6)	3 (1.1)
29 - 56	1 (1.5)	1 (1.5)	2 (3.0)	0	4 (1.4)
57 - 84	28 (41.8)	24 (35.3)	45 (67.2)	51 (67.1)	148 (53.2)
85 - 112	30 (44.8)	37 (54.4)	19 (28.4)	22 (28.9)	108 (38.8)
> 112	8 (11.9)	6 (8.8)	0	1 (1.3)	15 (5.4)
Duration (days)					
n	67	68	67	76	278
Mean (SD)	90.6 (13.45)	91.7 (14.31)	80.9 (10.52)	82.1 (11.24)	86.2 (13.29)
Median	86.0	86.5	84.0	84.0	84.0
Min, Max	56, 119	56, 120	28, 105	28, 114	28, 120

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] 00:59 <[redacted]>
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - 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=186) n (%)	600 mg IV (N=373) n (%)	1200 mg IV (N=372) n (%)	Total (N=745) n (%)	600 mg IV VS Placebo IV	1200 mg IV VS Placebo IV
Subjects with any treatment-emergent						
Adverse event (AE)	105 (56.5)	210 (56.3)	191 (51.3)	401 (53.8)	-0.2 (-8.9, 8.6)	-5.1 (-13.9, 3.6)
AE related to COVID-19	2 (1.1)	1 (0.3)	0	1 (0.1)	-0.8 (-2.4, 0.8)	-1.1 (-2.6, 0.4)
AE related to study drug according to the investigator	39 (21.0)	84 (22.5)	69 (18.5)	153 (20.5)	1.6 (-5.7, 8.8)	-2.4 (-9.5, 4.6)
Severe AE	18 (9.7)	22 (5.9)	18 (4.8)	40 (5.4)	-3.8 (-8.7, 1.1)	-4.8 (-9.6, -0.1)
Serious AE	28 (15.1)	27 (7.2)	14 (3.8)	41 (5.5)	-7.8 (-13.6, -2.0)	-11.3 (-16.8, -5.8)
AE leading to discontinuation of study drug	14 (7.5)	9 (2.4)	7 (1.9)	16 (2.1)	-5.1 (-9.2, -1.0)	-5.6 (-9.7, -1.6)
AE leading to death	2 (1.1)	0	0	0	-1.1 (-2.6, 0.4)	-1.1 (-2.6, 0.4)
All deaths						
Deaths occurring <= 140 days after last dose of study drug	2 (1.1)	0	0	0	-1.1 (-2.6, 0.4)	-1.1 (-2.6, 0.4)
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] 00:59 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - 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=67) n (%)	360 mg SC (N=68) n (%)	1200 mg IV (N=67) n (%)	1200 mg IV (N=76) n (%)	Total (N=278) n (%)
Subjects with any treatment-emergent					
Adverse event (AE)	31 (46.3)	34 (50.0)	35 (52.2)	40 (52.6)	140 (50.4)
AE related to COVID-19	1 (1.5)	0	1 (1.5)	0	2 (0.7)
AE related to study drug according to the investigator	9 (13.4)	15 (22.1)	9 (13.4)	17 (22.4)	50 (18.0)
Severe AE	2 (3.0)	4 (5.9)	3 (4.5)	5 (6.6)	14 (5.0)
Serious AE	3 (4.5)	3 (4.4)	4 (6.0)	4 (5.3)	14 (5.0)
AE leading to discontinuation of study drug	0	1 (1.5)	0	0	1 (0.4)
AE leading to death	0	0	0	0	0
All deaths					
Deaths occurring <= 140 days after last dose of study drug	0	0	0	0	0
Deaths occurring > 140 days after last dose of study drug	0	0	0	0	0
Deaths related to COVID-19	0	0	0	0	0

Note: Treatment-emergent AEs (TEAEs) for 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] 00:59 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 27

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
Any adverse event	105 (56.5)	210 (56.3)	191 (51.3)	401 (53.8)
血液およびリンパ系障害	10 (5.4)	16 (4.3)	14 (3.8)	30 (4.0)
貧血	6 (3.2)	11 (2.9)	10 (2.7)	21 (2.8)
凝血異常	1 (0.5)	0	0	0
好酸球増加症	1 (0.5)	0	0	0
内出血発生の増加傾向	0	1 (0.3)	0	1 (0.1)
鉄欠乏性貧血	1 (0.5)	0	1 (0.3)	1 (0.1)
白血球減少症	1 (0.5)	2 (0.5)	0	2 (0.3)
リンパ球減少症	1 (0.5)	2 (0.5)	1 (0.3)	3 (0.4)
小球性貧血	0	1 (0.3)	0	1 (0.1)
好中球減少症	0	1 (0.3)	1 (0.3)	2 (0.3)
好中球増加症	0	0	1 (0.3)	1 (0.1)
心臓障害	1 (0.5)	2 (0.5)	4 (1.1)	6 (0.8)
狭心症	0	1 (0.3)	0	1 (0.1)
不整脈	0	0	1 (0.3)	1 (0.1)
心房細動	0	0	1 (0.3)	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
心臓障害 (Cont.)				
心炎	1 (0.5)	0	0	0
動悸	0	0	1 (0.3)	1 (0.1)
頻脈	0	0	1 (0.3)	1 (0.1)
心室性頻脈	0	1 (0.3)	0	1 (0.1)
先天性、家族性および遺伝性障害	0	1 (0.3)	0	1 (0.1)
陰嚢水瘤	0	1 (0.3)	0	1 (0.1)
耳および迷路障害	2 (1.1)	5 (1.3)	2 (0.5)	7 (0.9)
耳痛	0	2 (0.5)	0	2 (0.3)
回転性めまい	2 (1.1)	3 (0.8)	2 (0.5)	5 (0.7)
内分泌障害	0	1 (0.3)	0	1 (0.1)
甲状腺腫瘤	0	1 (0.3)	0	1 (0.1)
眼障害	2 (1.1)	9 (2.4)	0	9 (1.2)
ドライアイ	0	2 (0.5)	0	2 (0.3)
眼痛	0	2 (0.5)	0	2 (0.3)
眼そう痒症	1 (0.5)	3 (0.8)	0	3 (0.4)
眼充血	1 (0.5)	1 (0.3)	0	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
眼障害 (Cont.)				
ぶどう膜炎	1 (0.5)	0	0	0
霧視	0	1 (0.3)	0	1 (0.1)
眼球乾燥症	0	1 (0.3)	0	1 (0.1)
胃腸障害	60 (32.3)	82 (22.0)	52 (14.0)	134 (18.0)
腹部膨満	2 (1.1)	1 (0.3)	7 (1.9)	8 (1.1)
腹部腫瘤	1 (0.5)	0	0	0
腹痛	10 (5.4)	8 (2.1)	10 (2.7)	18 (2.4)
下腹部痛	2 (1.1)	1 (0.3)	2 (0.5)	3 (0.4)
上腹部痛	3 (1.6)	2 (0.5)	3 (0.8)	5 (0.7)
腹部圧痛	0	0	1 (0.3)	1 (0.1)
裂肛	1 (0.5)	2 (0.5)	0	2 (0.3)
痔瘻	2 (1.1)	3 (0.8)	1 (0.3)	4 (0.5)
肛門狭窄	0	0	1 (0.3)	1 (0.1)
肛門直腸不快感	1 (0.5)	0	0	0
肛門直腸障害	1 (0.5)	0	0	0
アフタ性潰瘍	1 (0.5)	4 (1.1)	0	4 (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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
胃腸障害 (Cont.)				
口唇炎	0	0	1 (0.3)	1 (0.1)
大腸炎	1 (0.5)	0	1 (0.3)	1 (0.1)
便秘	0	7 (1.9)	0	7 (0.9)
クローン病	25 (13.4)	10 (2.7)	6 (1.6)	16 (2.1)
齲歯	1 (0.5)	0	0	0
下痢	4 (2.2)	2 (0.5)	5 (1.3)	7 (0.9)
血性下痢	1 (0.5)	0	0	0
腸憩室	0	1 (0.3)	0	1 (0.1)
口内乾燥	0	1 (0.3)	0	1 (0.1)
十二指腸潰瘍	1 (0.5)	0	0	0
十二指腸炎	1 (0.5)	0	0	0
細菌叢異常	1 (0.5)	0	0	0
消化不良	4 (2.2)	2 (0.5)	0	2 (0.3)
おくび	0	1 (0.3)	0	1 (0.1)
鼓腸	0	3 (0.8)	4 (1.1)	7 (0.9)
胃炎	2 (1.1)	1 (0.3)	1 (0.3)	2 (0.3)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
胃腸障害 (Cont.)				
びらん性胃炎	1 (0.5)	0	0	0
胃腸出血	0	1 (0.3)	0	1 (0.1)
胃腸の炎症	1 (0.5)	0	0	0
消化管壊死	1 (0.5)	0	0	0
胃食道逆流性疾患	3 (1.6)	3 (0.8)	1 (0.3)	4 (0.5)
歯肉痛	0	0	1 (0.3)	1 (0.1)
血便排泄	1 (0.5)	1 (0.3)	0	1 (0.1)
痔出血	0	1 (0.3)	0	1 (0.1)
裂孔ヘルニア	0	1 (0.3)	0	1 (0.1)
口の感覚鈍麻	0	0	1 (0.3)	1 (0.1)
回腸穿孔	1 (0.5)	0	0	0
回腸狭窄	0	0	1 (0.3)	1 (0.1)
イレウス	0	3 (0.8)	0	3 (0.4)
鼠径ヘルニア	0	1 (0.3)	0	1 (0.1)
腸閉塞	2 (1.1)	1 (0.3)	0	1 (0.1)
腸管狭窄	2 (1.1)	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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
胃腸障害 (Cont.)				
過敏性腸症候群	1 (0.5)	0	0	0
大腸狭窄	0	3 (0.8)	0	3 (0.4)
大腸穿孔	0	1 (0.3)	1 (0.3)	2 (0.3)
大腸ポリープ	0	3 (0.8)	1 (0.3)	4 (0.5)
口腔内潰瘍形成	0	4 (1.1)	0	4 (0.5)
悪心	10 (5.4)	17 (4.6)	13 (3.5)	30 (4.0)
非感染性歯肉炎	0	1 (0.3)	0	1 (0.1)
嚥下痛	0	0	2 (0.5)	2 (0.3)
食道潰瘍	0	1 (0.3)	0	1 (0.1)
口腔粘膜びらん	0	1 (0.3)	0	1 (0.1)
急性膵炎	0	1 (0.3)	0	1 (0.1)
口の錯感覚	0	1 (0.3)	0	1 (0.1)
肛門周囲痛	0	0	1 (0.3)	1 (0.1)
直腸分泌物	0	1 (0.3)	0	1 (0.1)
直腸出血	3 (1.6)	1 (0.3)	2 (0.5)	3 (0.4)
小腸閉塞	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
胃腸障害 (Cont.)				
口内炎	0	1 (0.3)	0	1 (0.1)
末端回腸炎	0	0	1 (0.3)	1 (0.1)
舌変色	0	1 (0.3)	0	1 (0.1)
舌潰瘍	0	1 (0.3)	0	1 (0.1)
歯痛	2 (1.1)	2 (0.5)	1 (0.3)	3 (0.4)
嘔吐	7 (3.8)	10 (2.7)	4 (1.1)	14 (1.9)
一般・全身障害および投与部位の状態	17 (9.1)	39 (10.5)	46 (12.4)	85 (11.4)
無力症	2 (1.1)	1 (0.3)	0	1 (0.1)
カテーテル留置部位漏出	0	1 (0.3)	0	1 (0.1)
カテーテル留置部位疼痛	1 (0.5)	0	0	0
胸部不快感	0	1 (0.3)	1 (0.3)	2 (0.3)
胸痛	1 (0.5)	0	1 (0.3)	1 (0.1)
悪寒	1 (0.5)	0	1 (0.3)	1 (0.1)
嚢胞	0	1 (0.3)	0	1 (0.1)
不快感	0	1 (0.3)	0	1 (0.1)
薬物不耐性	0	0	1 (0.3)	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
疲労	6 (3.2)	16 (4.3)	15 (4.0)	31 (4.2)
熱感	0	1 (0.3)	0	1 (0.1)
空腹	0	0	1 (0.3)	1 (0.1)
インフルエンザ様疾患	2 (1.1)	1 (0.3)	3 (0.8)	4 (0.5)
注入部位紅斑	0	1 (0.3)	0	1 (0.1)
注入部位刺激感	0	0	1 (0.3)	1 (0.1)
注入部位疼痛	0	0	1 (0.3)	1 (0.1)
注入部位腫脹	0	0	2 (0.5)	2 (0.3)
注射部位内出血	0	1 (0.3)	1 (0.3)	2 (0.3)
注射部位紅斑	0	0	1 (0.3)	1 (0.1)
注射部位疼痛	0	1 (0.3)	0	1 (0.1)
注射部位知覚異常	0	0	1 (0.3)	1 (0.1)
倦怠感	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)
浮腫	0	1 (0.3)	0	1 (0.1)
末梢性浮腫	1 (0.5)	2 (0.5)	0	2 (0.3)
疼痛	0	1 (0.3)	0	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
末梢腫脹	0	2 (0.5)	2 (0.5)	4 (0.5)
発熱	6 (3.2)	14 (3.8)	14 (3.8)	28 (3.8)
腫脹	0	0	2 (0.5)	2 (0.3)
全身性炎症反応症候群	0	0	1 (0.3)	1 (0.1)
肝胆道系障害	2 (1.1)	8 (2.1)	3 (0.8)	11 (1.5)
胆管結石	0	1 (0.3)	0	1 (0.1)
胆管炎	0	1 (0.3)	0	1 (0.1)
胆石症	1 (0.5)	1 (0.3)	0	1 (0.1)
薬物性肝障害	0	2 (0.5)	0	2 (0.3)
肝嚢胞	1 (0.5)	0	0	0
肝機能異常	1 (0.5)	3 (0.8)	1 (0.3)	4 (0.5)
肝脾腫大	0	1 (0.3)	0	1 (0.1)
肝毒性	0	0	1 (0.3)	1 (0.1)
肝障害	0	0	1 (0.3)	1 (0.1)
免疫系障害	1 (0.5)	2 (0.5)	3 (0.8)	5 (0.7)
食物アレルギー	0	1 (0.3)	0	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
免疫系障害 (Cont.)				
過敏症	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)
季節性アレルギー	0	0	2 (0.5)	2 (0.3)
感染症および寄生虫症	44 (23.7)	77 (20.6)	69 (18.5)	146 (19.6)
腹部膿瘍	1 (0.5)	0	0	0
腹壁膿瘍	1 (0.5)	0	0	0
腸管膿瘍	1 (0.5)	0	0	0
四肢膿瘍	0	0	1 (0.3)	1 (0.1)
肛門膿瘍	3 (1.6)	5 (1.3)	0	5 (0.7)
痔瘻感染	1 (0.5)	0	0	0
虫垂炎	0	1 (0.3)	0	1 (0.1)
無症候性COVID－19	1 (0.5)	0	0	0
細菌感染	0	0	1 (0.3)	1 (0.1)
細菌性膣症	0	1 (0.3)	1 (0.3)	2 (0.3)
気管支炎	2 (1.1)	2 (0.5)	4 (1.1)	6 (0.8)
COVID－19	1 (0.5)	1 (0.3)	0	1 (0.1)
COVID－19肺炎	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.

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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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
感染症および寄生虫症 (Cont.)				
カンジダ感染	1 (0.5)	0	1 (0.3)	1 (0.1)
蜂巣炎	1 (0.5)	0	0	0
結膜炎	1 (0.5)	1 (0.3)	2 (0.5)	3 (0.4)
膀胱炎	0	2 (0.5)	1 (0.3)	3 (0.4)
サイトメガロウイルス感染	0	0	1 (0.3)	1 (0.1)
医療機器関連敗血症	1 (0.5)	0	0	0
耳感染	0	0	1 (0.3)	1 (0.1)
精巣上体炎	0	0	1 (0.3)	1 (0.1)
毛包炎	0	1 (0.3)	0	1 (0.1)
胃腸炎	2 (1.1)	3 (0.8)	2 (0.5)	5 (0.7)
ウイルス性胃腸炎	0	1 (0.3)	3 (0.8)	4 (0.5)
陰部ヘルペス	0	1 (0.3)	0	1 (0.1)
真菌性性器感染	0	1 (0.3)	0	1 (0.1)
歯肉炎	1 (0.5)	0	0	0
単純ヘルペス	0	1 (0.3)	0	1 (0.1)
ヘルペスウイルス感染	0	0	1 (0.3)	1 (0.1)

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.
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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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
感染症および寄生虫症 (Cont.)				
帯状疱疹	0	2 (0.5)	1 (0.3)	3 (0.4)
麦粒腫	0	0	1 (0.3)	1 (0.1)
膿痂疹	0	0	1 (0.3)	1 (0.1)
インフルエンザ	2 (1.1)	4 (1.1)	2 (0.5)	6 (0.8)
注入部位蜂巣炎	0	0	1 (0.3)	1 (0.1)
関節膿瘍	0	0	1 (0.3)	1 (0.1)
大腸感染	0	1 (0.3)	0	1 (0.1)
喉頭炎	0	1 (0.3)	0	1 (0.1)
レプトスピラ症	0	1 (0.3)	0	1 (0.1)
限局性感染	0	1 (0.3)	0	1 (0.1)
下気道感染	1 (0.5)	2 (0.5)	0	2 (0.3)
鼻前庭炎	1 (0.5)	0	0	0
上咽頭炎	5 (2.7)	22 (5.9)	22 (5.9)	44 (5.9)
口腔カンジダ症	1 (0.5)	1 (0.3)	0	1 (0.1)
口腔ヘルペス	1 (0.5)	0	4 (1.1)	4 (0.5)
爪囲炎	0	1 (0.3)	1 (0.3)	2 (0.3)

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.
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TABLE 14.3__1.1.2.3

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and Preferred Term during the 12-Week Induction Period
(SA1 Population)

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感染症および寄生虫症 (Cont.)				
歯周炎	0	1 (0.3)	0	1 (0.1)
腹膜炎	0	1 (0.3)	0	1 (0.1)
咽頭炎	1 (0.5)	2 (0.5)	2 (0.5)	4 (0.5)
レンサ球菌性咽頭炎	1 (0.5)	0	3 (0.8)	3 (0.4)
肺炎	4 (2.2)	1 (0.3)	3 (0.8)	4 (0.5)
術後創感染	1 (0.5)	0	0	0
肺敗血症	1 (0.5)	0	0	0
肺結核	1 (0.5)	0	0	0
歯髄炎	1 (0.5)	0	0	0
腎盂腎炎	1 (0.5)	0	0	0
ウイルス性気道感染	0	1 (0.3)	1 (0.3)	2 (0.3)
鼻炎	1 (0.5)	3 (0.8)	3 (0.8)	6 (0.8)
副鼻腔炎	3 (1.6)	5 (1.3)	1 (0.3)	6 (0.8)
皮膚感染	0	0	1 (0.3)	1 (0.1)
扁桃炎	1 (0.5)	0	1 (0.3)	1 (0.1)
歯膿瘍	1 (0.5)	0	2 (0.5)	2 (0.3)

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.
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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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
感染症および寄生虫症 (Cont.)				
歯感染	1 (0.5)	0	0	0
気管炎	0	2 (0.5)	0	2 (0.3)
結核	0	1 (0.3)	0	1 (0.1)
上気道感染	2 (1.1)	11 (2.9)	12 (3.2)	23 (3.1)
尿路感染	1 (0.5)	1 (0.3)	3 (0.8)	4 (0.5)
ウイルス感染	1 (0.5)	1 (0.3)	4 (1.1)	5 (0.7)
ウイルス性咽頭炎	1 (0.5)	0	0	0
ウイルス性上気道感染	2 (1.1)	0	0	0
外陰部膿瘍	1 (0.5)	0	0	0
女性外陰部蜂巣炎	1 (0.5)	0	0	0
外陰腟真菌感染	0	0	1 (0.3)	1 (0.1)
傷害、中毒および処置合併症	6 (3.2)	10 (2.7)	13 (3.5)	23 (3.1)
労働災害	0	0	1 (0.3)	1 (0.1)
肛門損傷	0	1 (0.3)	0	1 (0.1)
胸部損傷	0	1 (0.3)	0	1 (0.1)
挫傷	0	2 (0.5)	4 (1.1)	6 (0.8)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
傷害、中毒および処置合併症 (Cont.)				
歯科修復不成功	0	1 (0.3)	0	1 (0.1)
転倒	0	2 (0.5)	0	2 (0.3)
足骨折	0	1 (0.3)	0	1 (0.1)
前腕骨折	0	1 (0.3)	0	1 (0.1)
注入に伴う反応	1 (0.5)	2 (0.5)	1 (0.3)	3 (0.4)
損傷	0	0	1 (0.3)	1 (0.1)
関節脱臼	1 (0.5)	0	0	0
四肢損傷	1 (0.5)	0	1 (0.3)	1 (0.1)
筋損傷	1 (0.5)	0	0	0
口腔挫傷	0	1 (0.3)	0	1 (0.1)
処置後出血	0	0	1 (0.3)	1 (0.1)
処置による疼痛	1 (0.5)	0	1 (0.3)	1 (0.1)
橈骨骨折	0	0	1 (0.3)	1 (0.1)
肋骨骨折	0	0	1 (0.3)	1 (0.1)
交通事故	1 (0.5)	0	0	0
引っかき傷	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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
傷害、中毒および処置合併症 (Cont.)				
皮膚擦過傷	0	1 (0.3)	0	1 (0.1)
皮膚裂傷	0	0	2 (0.5)	2 (0.3)
創傷	0	0	1 (0.3)	1 (0.1)
創離開	1 (0.5)	0	0	0
臨床検査	8 (4.3)	11 (2.9)	20 (5.4)	31 (4.2)
アラニンアミノトランスフェラーゼ増加	1 (0.5)	0	2 (0.5)	2 (0.3)
アミラーゼ増加	0	0	1 (0.3)	1 (0.1)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (0.3)	1 (0.3)	2 (0.3)
血中アルカリホスファターゼ増加	0	2 (0.5)	0	2 (0.3)
血中ブドウ糖増加	0	0	1 (0.3)	1 (0.1)
血中リン減少	0	2 (0.5)	0	2 (0.3)
血中トリグリセリド増加	1 (0.5)	0	0	0
尿中血陽性	0	0	1 (0.3)	1 (0.1)
体温上昇	0	0	2 (0.5)	2 (0.3)
γ－グルタミルトランスフェラーゼ増加	0	3 (0.8)	0	3 (0.4)
ヘモグロビン減少	0	0	2 (0.5)	2 (0.3)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
臨床検査 (Cont.)				
ヘリコバクター検査陽性	1 (0.5)	0	0	0
肝酵素上昇	1 (0.5)	0	0	0
ホルモン値異常	0	0	1 (0.3)	1 (0.1)
リパーゼ増加	0	0	1 (0.3)	1 (0.1)
肝機能検査異常	0	1 (0.3)	0	1 (0.1)
低比重リポ蛋白減少	0	0	1 (0.3)	1 (0.1)
リンパ球数減少	0	2 (0.5)	2 (0.5)	4 (0.5)
QRS軸異常	0	0	1 (0.3)	1 (0.1)
サルモネラ検査陽性	0	0	1 (0.3)	1 (0.1)
血清フェリチン減少	1 (0.5)	1 (0.3)	0	1 (0.1)
トランスアミナーゼ上昇	0	0	1 (0.3)	1 (0.1)
体重減少	1 (0.5)	1 (0.3)	0	1 (0.1)
体重増加	2 (1.1)	1 (0.3)	2 (0.5)	3 (0.4)
白血球数減少	0	0	3 (0.8)	3 (0.4)
代謝および栄養障害	6 (3.2)	7 (1.9)	6 (1.6)	13 (1.7)
食欲減退	0	1 (0.3)	0	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
代謝および栄養障害 (Cont.)				
脱水	0	0	2 (0.5)	2 (0.3)
糖尿病	0	2 (0.5)	1 (0.3)	3 (0.4)
電解質失調	1 (0.5)	0	0	0
葉酸欠乏	0	0	1 (0.3)	1 (0.1)
高血糖	1 (0.5)	0	0	0
高カリウム血症	1 (0.5)	0	0	0
高脂血症	0	1 (0.3)	1 (0.3)	2 (0.3)
低アルブミン血症	1 (0.5)	0	0	0
低カリウム血症	0	2 (0.5)	2 (0.5)	4 (0.5)
低マグネシウム血症	0	0	1 (0.3)	1 (0.1)
鉄欠乏	2 (1.1)	0	0	0
ビタミンB12欠乏	0	0	1 (0.3)	1 (0.1)
ビタミンD欠乏	1 (0.5)	0	0	0
亜鉛欠乏	0	1 (0.3)	0	1 (0.1)
筋骨格系および結合組織障害	21 (11.3)	38 (10.2)	30 (8.1)	68 (9.1)
強直性脊椎炎	0	1 (0.3)	0	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
筋骨格系および結合組織障害 (Cont.)				
関節痛	7 (3.8)	15 (4.0)	11 (3.0)	26 (3.5)
関節炎	0	1 (0.3)	0	1 (0.1)
関節障害	5 (2.7)	5 (1.3)	2 (0.5)	7 (0.9)
軸性脊椎関節炎	0	1 (0.3)	1 (0.3)	2 (0.3)
背部痛	1 (0.5)	4 (1.1)	6 (1.6)	10 (1.3)
骨痛	0	0	1 (0.3)	1 (0.1)
滑液包炎	0	0	1 (0.3)	1 (0.1)
線維筋痛	1 (0.5)	1 (0.3)	0	1 (0.1)
瘻孔	1 (0.5)	0	1 (0.3)	1 (0.1)
側腹部痛	1 (0.5)	1 (0.3)	0	1 (0.1)
関節強直	0	1 (0.3)	0	1 (0.1)
関節硬直	1 (0.5)	0	0	0
若年性特発性関節炎	0	1 (0.3)	0	1 (0.1)
筋拘縮	1 (0.5)	0	0	0
筋痙縮	2 (1.1)	0	2 (0.5)	2 (0.3)
筋骨格系胸痛	0	2 (0.5)	0	2 (0.3)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
筋骨格系および結合組織障害 (Cont.)				
筋骨格痛	0	1 (0.3)	0	1 (0.1)
筋肉痛	0	5 (1.3)	4 (1.1)	9 (1.2)
頚部痛	0	2 (0.5)	1 (0.3)	3 (0.4)
骨炎	1 (0.5)	0	0	0
変形性関節症	0	1 (0.3)	0	1 (0.1)
骨減少症	0	1 (0.3)	0	1 (0.1)
四肢痛	0	4 (1.1)	1 (0.3)	5 (0.7)
脊椎炎	2 (1.1)	0	0	0
脊椎関節障害	0	1 (0.3)	1 (0.3)	2 (0.3)
腱炎	1 (0.5)	0	0	0
腱鞘炎	0	1 (0.3)	0	1 (0.1)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.5)	3 (0.8)	0	3 (0.4)
アクロコルドン	0	1 (0.3)	0	1 (0.1)
肛門性器疣贅	0	1 (0.3)	0	1 (0.1)
皮膚乳頭腫	1 (0.5)	1 (0.3)	0	1 (0.1)
神経系障害	14 (7.5)	38 (10.2)	36 (9.7)	74 (9.9)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
神経系障害 (Cont.)				
手根管症候群	0	0	1 (0.3)	1 (0.1)
浮動性めまい	2 (1.1)	9 (2.4)	10 (2.7)	19 (2.6)
味覚不全	1 (0.5)	1 (0.3)	0	1 (0.1)
顔面麻痺	0	1 (0.3)	0	1 (0.1)
頭痛	8 (4.3)	24 (6.4)	20 (5.4)	44 (5.9)
感覚鈍麻	0	0	2 (0.5)	2 (0.3)
嗜眠	0	3 (0.8)	1 (0.3)	4 (0.5)
記憶障害	0	1 (0.3)	0	1 (0.1)
片頭痛	1 (0.5)	4 (1.1)	1 (0.3)	5 (0.7)
錯感覚	1 (0.5)	1 (0.3)	0	1 (0.1)
失神寸前の状態	0	0	1 (0.3)	1 (0.1)
坐骨神経痛	0	1 (0.3)	1 (0.3)	2 (0.3)
睡眠時麻痺	0	0	1 (0.3)	1 (0.1)
傾眠	0	0	1 (0.3)	1 (0.1)
失神	1 (0.5)	0	0	0
振戦	0	1 (0.3)	0	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
精神障害	2 (1.1)	8 (2.1)	13 (3.5)	21 (2.8)
感情障害	0	1 (0.3)	0	1 (0.1)
不安	1 (0.5)	0	4 (1.1)	4 (0.5)
気晴らし食い	0	1 (0.3)	0	1 (0.1)
抑うつ気分	0	0	1 (0.3)	1 (0.1)
うつ病	0	0	4 (1.1)	4 (0.5)
失見当識	1 (0.5)	0	0	0
不眠症	0	5 (1.3)	5 (1.3)	10 (1.3)
神経過敏	0	1 (0.3)	0	1 (0.1)
悪夢	0	0	1 (0.3)	1 (0.1)
睡眠障害	0	1 (0.3)	0	1 (0.1)
腎および尿路障害	2 (1.1)	4 (1.1)	5 (1.3)	9 (1.2)
膀胱刺激症状	0	0	1 (0.3)	1 (0.1)
排尿困難	0	0	1 (0.3)	1 (0.1)
血尿	0	1 (0.3)	0	1 (0.1)
水腎症	0	1 (0.3)	0	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
腎および尿路障害 (Cont.)				
尿意切迫	0	1 (0.3)	0	1 (0.1)
腎結石症	1 (0.5)	0	2 (0.5)	2 (0.3)
腎仙痛	0	0	1 (0.3)	1 (0.1)
腎尿細管障害	1 (0.5)	0	0	0
尿管結石症	0	2 (0.5)	0	2 (0.3)
生殖系および乳房障害	1 (0.5)	4 (1.1)	4 (1.1)	8 (1.1)
乳房分泌	0	0	1 (0.3)	1 (0.1)
乳房障害	0	1 (0.3)	0	1 (0.1)
乳房痛	0	1 (0.3)	0	1 (0.1)
子宮頚部上皮異形成	1 (0.5)	0	0	0
月経困難症	0	1 (0.3)	1 (0.3)	2 (0.3)
不正子宮出血	0	0	1 (0.3)	1 (0.1)
前立腺炎	0	1 (0.3)	0	1 (0.1)
陰嚢皮膚炎	0	0	1 (0.3)	1 (0.1)
呼吸器、胸郭および縦隔障害	10 (5.4)	14 (3.8)	10 (2.7)	24 (3.2)
失声症	0	0	1 (0.3)	1 (0.1)

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.
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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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
喘息	0	2 (0.5)	0	2 (0.3)
気管支痙攣	0	0	1 (0.3)	1 (0.1)
咳嗽	4 (2.2)	4 (1.1)	0	4 (0.5)
呼吸困難	1 (0.5)	2 (0.5)	2 (0.5)	4 (0.5)
労作性呼吸困難	1 (0.5)	1 (0.3)	0	1 (0.1)
鼻出血	0	1 (0.3)	2 (0.5)	3 (0.4)
しゃっくり	0	1 (0.3)	0	1 (0.1)
鼻閉	0	1 (0.3)	1 (0.3)	2 (0.3)
鼻部不快感	0	0	1 (0.3)	1 (0.1)
鼻中隔弯曲	0	0	1 (0.3)	1 (0.1)
鼻甲介肥大	0	0	1 (0.3)	1 (0.1)
鼻潰瘍	1 (0.5)	1 (0.3)	0	1 (0.1)
口腔咽頭痛	4 (2.2)	2 (0.5)	2 (0.5)	4 (0.5)
湿性咳嗽	0	2 (0.5)	1 (0.3)	3 (0.4)
肺塞栓症	0	0	1 (0.3)	1 (0.1)
アレルギー性鼻炎	0	1 (0.3)	0	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
鼻漏	0	2 (0.5)	0	2 (0.3)
上気道の炎症	1 (0.5)	0	0	0
皮膚および皮下組織障害	10 (5.4)	39 (10.5)	34 (9.1)	73 (9.8)
ざ瘡	2 (1.1)	2 (0.5)	3 (0.8)	5 (0.7)
脱毛症	0	9 (2.4)	2 (0.5)	11 (1.5)
水疱	1 (0.5)	1 (0.3)	0	1 (0.1)
皮膚症	0	0	1 (0.3)	1 (0.1)
皮膚乾燥	0	1 (0.3)	0	1 (0.1)
異汗性湿疹	0	1 (0.3)	0	1 (0.1)
湿疹	1 (0.5)	2 (0.5)	5 (1.3)	7 (0.9)
紅斑	1 (0.5)	1 (0.3)	5 (1.3)	6 (0.8)
結節性紅斑	0	2 (0.5)	1 (0.3)	3 (0.4)
多汗症	0	1 (0.3)	0	1 (0.1)
間擦疹	0	0	1 (0.3)	1 (0.1)
硬化性苔癬	1 (0.5)	0	0	0
斑	0	0	1 (0.3)	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
皮膚および皮下組織障害 (Cont.)				
寝汗	0	2 (0.5)	0	2 (0.3)
爪破損	0	1 (0.3)	0	1 (0.1)
爪甲剥離症	0	1 (0.3)	0	1 (0.1)
丘疹	0	0	1 (0.3)	1 (0.1)
光線過敏性反応	0	1 (0.3)	2 (0.5)	3 (0.4)
痒疹	0	1 (0.3)	0	1 (0.1)
そう痒症	1 (0.5)	4 (1.1)	5 (1.3)	9 (1.2)
乾癬	1 (0.5)	0	1 (0.3)	1 (0.1)
発疹	2 (1.1)	12 (3.2)	4 (1.1)	16 (2.1)
斑状皮疹	1 (0.5)	0	0	0
斑状丘疹状皮疹	0	0	1 (0.3)	1 (0.1)
丘疹性皮疹	0	0	1 (0.3)	1 (0.1)
そう痒性皮疹	1 (0.5)	0	0	0
酒さ	0	1 (0.3)	1 (0.3)	2 (0.3)
脂漏性皮膚炎	0	1 (0.3)	2 (0.5)	3 (0.4)
皮膚出血	0	1 (0.3)	0	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
皮膚および皮下組織障害 (Cont.)				
皮膚病変	0	0	1 (0.3)	1 (0.1)
蕁麻疹	1 (0.5)	0	1 (0.3)	1 (0.1)
外科および内科処置	0	1 (0.3)	0	1 (0.1)
人工流産	0	1 (0.3)	0	1 (0.1)
血管障害	3 (1.6)	10 (2.7)	8 (2.2)	18 (2.4)
深部静脈血栓症	0	0	1 (0.3)	1 (0.1)
潮紅	0	1 (0.3)	0	1 (0.1)
血腫	1 (0.5)	0	0	0
ほてり	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)
高血圧	1 (0.5)	6 (1.6)	4 (1.1)	10 (1.3)
低血圧	0	1 (0.3)	0	1 (0.1)
起立性低血圧	0	0	1 (0.3)	1 (0.1)
収縮期高血圧	0	0	1 (0.3)	1 (0.1)
血栓性静脈炎	0	1 (0.3)	0	1 (0.1)

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

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RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - 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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
Any adverse event	31 (46.3)	34 (50.0)	35 (52.2)	40 (52.6)	140 (50.4)
血液およびリンパ系障害	0	5 (7.4)	3 (4.5)	5 (6.6)	13 (4.7)
貧血	0	2 (2.9)	1 (1.5)	4 (5.3)	7 (2.5)
鉄欠乏性貧血	0	1 (1.5)	0	0	1 (0.4)
白血球減少症	0	0	0	1 (1.3)	1 (0.4)
リンパ球減少症	0	2 (2.9)	1 (1.5)	0	3 (1.1)
骨髄抑制	0	0	1 (1.5)	0	1 (0.4)
心臓障害	1 (1.5)	0	0	0	1 (0.4)
動悸	1 (1.5)	0	0	0	1 (0.4)
先天性、家族性および遺伝性障害	1 (1.5)	0	0	0	1 (0.4)
重複腎	1 (1.5)	0	0	0	1 (0.4)
眼障害	0	1 (1.5)	1 (1.5)	3 (3.9)	5 (1.8)
眼瞼炎	0	0	0	1 (1.3)	1 (0.4)
眼瞼痙攣	0	1 (1.5)	0	0	1 (0.4)
羞明	0	0	0	1 (1.3)	1 (0.4)
網膜障害	0	0	0	1 (1.3)	1 (0.4)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
眼障害 (Cont.)					
ぶどう膜炎	0	0	1 (1.5)	0	1 (0.4)
胃腸障害	10 (14.9)	14 (20.6)	10 (14.9)	10 (13.2)	44 (15.8)
腹部不快感	0	1 (1.5)	0	0	1 (0.4)
腹部膨満	0	0	1 (1.5)	0	1 (0.4)
腹部ヘルニア	0	0	1 (1.5)	0	1 (0.4)
腹部腫瘤	0	0	1 (1.5)	0	1 (0.4)
腹痛	1 (1.5)	0	1 (1.5)	1 (1.3)	3 (1.1)
上腹部痛	0	1 (1.5)	0	0	1 (0.4)
腹部圧痛	0	0	1 (1.5)	0	1 (0.4)
後天性食道ウエッブ	1 (1.5)	0	0	0	1 (0.4)
裂肛	0	1 (1.5)	1 (1.5)	1 (1.3)	3 (1.1)
痔瘻	0	1 (1.5)	1 (1.5)	0	2 (0.7)
アフタ性潰瘍	2 (3.0)	1 (1.5)	0	0	3 (1.1)
バレット食道	1 (1.5)	0	0	0	1 (0.4)
クローン病	3 (4.5)	1 (1.5)	0	1 (1.3)	5 (1.8)
下痢	1 (1.5)	1 (1.5)	1 (1.5)	2 (2.6)	5 (1.8)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
胃腸障害 (Cont.)					
消化不良	0	0	1 (1.5)	1 (1.3)	2 (0.7)
嚥下障害	1 (1.5)	0	0	0	1 (0.4)
小腸炎	0	0	0	1 (1.3)	1 (0.4)
好酸球性食道炎	1 (1.5)	0	0	0	1 (0.4)
鼓腸	0	1 (1.5)	0	0	1 (0.4)
消化管壊死	0	0	1 (1.5)	0	1 (0.4)
胃腸音異常	0	0	0	1 (1.3)	1 (0.4)
胃食道逆流性疾患	0	1 (1.5)	0	1 (1.3)	2 (0.7)
血便排泄	0	1 (1.5)	0	2 (2.6)	3 (1.1)
血栓性痔核	0	1 (1.5)	0	0	1 (0.4)
腸管虚血	0	0	1 (1.5)	0	1 (0.4)
腸閉塞	1 (1.5)	1 (1.5)	0	1 (1.3)	3 (1.1)
腸管ポリープ	0	1 (1.5)	0	0	1 (0.4)
過敏性腸症候群	0	0	1 (1.5)	0	1 (0.4)
大腸穿孔	0	1 (1.5)	0	0	1 (0.4)
悪心	1 (1.5)	0	0	3 (3.9)	4 (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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
胃腸障害 (Cont.)					
肛門周囲痛	0	1 (1.5)	0	0	1 (0.4)
直腸異形成	0	1 (1.5)	0	0	1 (0.4)
直腸しぶり	0	1 (1.5)	0	0	1 (0.4)
小腸閉塞	0	0	1 (1.5)	0	1 (0.4)
亜イレウス	0	0	0	1 (1.3)	1 (0.4)
嘔吐	2 (3.0)	1 (1.5)	2 (3.0)	0	5 (1.8)
一般・全身障害および投与部位の状態	2 (3.0)	4 (5.9)	5 (7.5)	8 (10.5)	19 (6.8)
無力症	0	0	0	2 (2.6)	2 (0.7)
胸部不快感	1 (1.5)	0	0	0	1 (0.4)
胸痛	0	0	0	1 (1.3)	1 (0.4)
分泌	1 (1.5)	0	0	0	1 (0.4)
疲労	0	2 (2.9)	0	3 (3.9)	5 (1.8)
インフルエンザ様疾患	0	1 (1.5)	1 (1.5)	0	2 (0.7)
注入部位紅斑	0	0	1 (1.5)	0	1 (0.4)
注入部位腫脹	0	0	0	1 (1.3)	1 (0.4)
注射部位紅斑	0	0	0	1 (1.3)	1 (0.4)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
注射部位疼痛	0	0	1 (1.5)	0	1 (0.4)
注射部位腫脹	0	1 (1.5)	1 (1.5)	0	2 (0.7)
注射部位熱感	0	0	0	1 (1.3)	1 (0.4)
発熱	0	1 (1.5)	1 (1.5)	0	2 (0.7)
肝胆道系障害	1 (1.5)	0	1 (1.5)	0	2 (0.7)
急性胆嚢炎	0	0	1 (1.5)	0	1 (0.4)
胆嚢障害	1 (1.5)	0	0	0	1 (0.4)
免疫系障害	0	1 (1.5)	1 (1.5)	0	2 (0.7)
薬物過敏症	0	0	1 (1.5)	0	1 (0.4)
過敏症	0	1 (1.5)	0	0	1 (0.4)
感染症および寄生虫症	9 (13.4)	13 (19.1)	13 (19.4)	11 (14.5)	46 (16.5)
気管支炎	1 (1.5)	2 (2.9)	1 (1.5)	1 (1.3)	5 (1.8)
COVID－19	1 (1.5)	0	1 (1.5)	0	2 (0.7)
COVID－19肺炎	0	0	1 (1.5)	0	1 (0.4)
結膜炎	1 (1.5)	0	0	0	1 (0.4)
膀胱炎	1 (1.5)	0	0	0	1 (0.4)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
感染症および寄生虫症 (Cont.)					
エンテロバクター感染	0	0	1 (1.5)	0	1 (0.4)
大腸菌性尿路感染	0	1 (1.5)	0	0	1 (0.4)
毛包炎	0	0	1 (1.5)	0	1 (0.4)
胃腸炎	1 (1.5)	0	2 (3.0)	0	3 (1.1)
ノロウイルス性胃腸炎	0	0	0	1 (1.3)	1 (0.4)
ヘリコバクター感染	0	0	0	1 (1.3)	1 (0.4)
単純ヘルペス	1 (1.5)	0	1 (1.5)	0	2 (0.7)
帯状疱疹	0	1 (1.5)	0	0	1 (0.4)
インフルエンザ	0	3 (4.4)	0	0	3 (1.1)
上咽頭炎	1 (1.5)	1 (1.5)	1 (1.5)	2 (2.6)	5 (1.8)
中耳炎	0	1 (1.5)	0	0	1 (0.4)
会陰膿瘍	0	0	0	1 (1.3)	1 (0.4)
腹膜炎	0	1 (1.5)	0	0	1 (0.4)
細菌性咽頭炎	0	1 (1.5)	0	0	1 (0.4)
ヘルペス性直腸炎	0	0	0	1 (1.3)	1 (0.4)
ウイルス性気道感染	0	0	0	1 (1.3)	1 (0.4)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
感染症および寄生虫症 (Cont.)					
鼻炎	0	0	1 (1.5)	1 (1.3)	2 (0.7)
ライノウイルス感染	0	0	1 (1.5)	0	1 (0.4)
皮膚カンジダ	0	0	0	1 (1.3)	1 (0.4)
ブドウ球菌皮膚感染	1 (1.5)	0	0	0	1 (0.4)
足部白癬	0	0	1 (1.5)	0	1 (0.4)
癜風	0	0	0	1 (1.3)	1 (0.4)
扁桃炎	0	0	0	1 (1.3)	1 (0.4)
気管気管支炎	0	0	0	1 (1.3)	1 (0.4)
上気道感染	2 (3.0)	3 (4.4)	0	1 (1.3)	6 (2.2)
尿路感染	1 (1.5)	0	1 (1.5)	0	2 (0.7)
腟感染	0	0	1 (1.5)	0	1 (0.4)
ウイルス感染	0	0	1 (1.5)	0	1 (0.4)
ウイルス性上気道感染	0	1 (1.5)	0	0	1 (0.4)
外陰部腟カンジダ症	0	0	1 (1.5)	0	1 (0.4)
外陰腟炎	0	0	1 (1.5)	0	1 (0.4)
膿創	0	0	1 (1.5)	0	1 (0.4)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
傷害、中毒および処置合併症	2 (3.0)	2 (2.9)	2 (3.0)	6 (7.9)	12 (4.3)
吻合部漏出	0	0	0	1 (1.3)	1 (0.4)
動物による引っかき傷	0	0	1 (1.5)	0	1 (0.4)
挫傷	1 (1.5)	0	0	0	1 (0.4)
注入に伴う反応	0	0	0	1 (1.3)	1 (0.4)
関節損傷	0	0	0	1 (1.3)	1 (0.4)
靭帯捻挫	0	1 (1.5)	0	1 (1.3)	2 (0.7)
処置後出血	0	0	0	1 (1.3)	1 (0.4)
処置後低血圧	0	0	1 (1.5)	0	1 (0.4)
肋骨骨折	0	0	0	1 (1.3)	1 (0.4)
瘢痕	0	1 (1.5)	0	0	1 (0.4)
皮膚裂傷	1 (1.5)	0	0	0	1 (0.4)
臨床検査	2 (3.0)	2 (2.9)	5 (7.5)	1 (1.3)	10 (3.6)
アラニンアミノトランスフェラーゼ増加	0	0	2 (3.0)	0	2 (0.7)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (1.5)	0	1 (0.4)
血中アルカリホスファターゼ増加	0	0	1 (1.5)	0	1 (0.4)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
臨床検査 (Cont.)					
血中クレアチンホスホキナーゼ増加	1 (1.5)	0	0	0	1 (0.4)
γ-グルタミルトランスフェラーゼ増加	0	0	2 (3.0)	0	2 (0.7)
肝酵素上昇	0	0	0	1 (1.3)	1 (0.4)
リンパ球数減少	0	1 (1.5)	0	0	1 (0.4)
好中球百分率増加	0	0	1 (1.5)	0	1 (0.4)
血小板数減少	1 (1.5)	1 (1.5)	0	0	2 (0.7)
白血球数減少	0	0	1 (1.5)	0	1 (0.4)
代謝および栄養障害	2 (3.0)	2 (2.9)	2 (3.0)	2 (2.6)	8 (2.9)
葉酸欠乏	1 (1.5)	0	0	0	1 (0.4)
高トリグリセリド血症	0	0	1 (1.5)	1 (1.3)	2 (0.7)
低カリウム血症	0	1 (1.5)	1 (1.5)	0	2 (0.7)
低リン酸血症	0	0	0	1 (1.3)	1 (0.4)
多飲症	1 (1.5)	0	0	0	1 (0.4)
ビタミンB12欠乏	0	1 (1.5)	0	0	1 (0.4)
筋骨格系および結合組織障害	4 (6.0)	4 (5.9)	6 (9.0)	9 (11.8)	23 (8.3)
関節痛	3 (4.5)	0	2 (3.0)	3 (3.9)	8 (2.9)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
筋骨格系および結合組織障害 (Cont.)					
関節炎	0	0	0	1 (1.3)	1 (0.4)
関節障害	0	1 (1.5)	0	2 (2.6)	3 (1.1)
背部痛	1 (1.5)	2 (2.9)	1 (1.5)	1 (1.3)	5 (1.8)
瘻孔	0	0	0	1 (1.3)	1 (0.4)
側腹部痛	0	0	1 (1.5)	0	1 (0.4)
関節腫脹	0	0	0	1 (1.3)	1 (0.4)
筋肉痛	0	1 (1.5)	2 (3.0)	1 (1.3)	4 (1.4)
変形性関節症	1 (1.5)	0	0	0	1 (0.4)
肩回旋筋腱板症候群	1 (1.5)	0	0	0	1 (0.4)
仙腸骨炎	0	0	0	1 (1.3)	1 (0.4)
腱炎	0	0	1 (1.5)	0	1 (0.4)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (1.5)	1 (1.5)	1 (1.5)	2 (2.6)	5 (1.8)
基底細胞癌	0	0	0	1 (1.3)	1 (0.4)
大腸腺腫	0	1 (1.5)	0	0	1 (0.4)
脂肪腫	1 (1.5)	0	0	0	1 (0.4)
メラノサイト性母斑	0	0	1 (1.5)	0	1 (0.4)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) 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.)					
脂漏性角化症	0	0	1 (1.5)	0	1 (0.4)
外陰膣部疣贅	0	0	0	1 (1.3)	1 (0.4)
神経系障害	5 (7.5)	4 (5.9)	3 (4.5)	9 (11.8)	21 (7.6)
アカシジア	0	0	1 (1.5)	0	1 (0.4)
浮動性めまい	0	0	0	3 (3.9)	3 (1.1)
味覚不全	0	0	0	1 (1.3)	1 (0.4)
頭痛	1 (1.5)	3 (4.4)	2 (3.0)	5 (6.6)	11 (4.0)
感覚鈍麻	0	1 (1.5)	0	0	1 (0.4)
嗜眠	1 (1.5)	0	0	0	1 (0.4)
片頭痛	1 (1.5)	0	0	0	1 (0.4)
錯感覚	1 (1.5)	0	0	1 (1.3)	2 (0.7)
坐骨神経痛	1 (1.5)	0	0	0	1 (0.4)
味覚障害	1 (1.5)	0	0	0	1 (0.4)
精神障害	0	2 (2.9)	2 (3.0)	2 (2.6)	6 (2.2)
適応障害	0	1 (1.5)	0	0	1 (0.4)
不安	0	1 (1.5)	0	0	1 (0.4)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
精神障害 (Cont.)					
うつ病	0	1 (1.5)	0	0	1 (0.4)
不眠症	0	1 (1.5)	1 (1.5)	2 (2.6)	4 (1.4)
精神障害	0	1 (1.5)	0	0	1 (0.4)
強迫性障害	0	0	1 (1.5)	0	1 (0.4)
腎および尿路障害	3 (4.5)	0	1 (1.5)	1 (1.3)	5 (1.8)
尿路結石	2 (3.0)	0	0	0	2 (0.7)
腎結石症	0	0	0	1 (1.3)	1 (0.4)
腎嚢胞	1 (1.5)	0	0	0	1 (0.4)
腎臓痛	1 (1.5)	0	0	0	1 (0.4)
尿管結石症	0	0	1 (1.5)	0	1 (0.4)
生殖系および乳房障害	1 (1.5)	1 (1.5)	1 (1.5)	1 (1.3)	4 (1.4)
無月経	0	0	1 (1.5)	0	1 (0.4)
月経過多	0	0	0	1 (1.3)	1 (0.4)
希発月経	0	1 (1.5)	0	0	1 (0.4)
卵巣嚢胞	1 (1.5)	0	0	0	1 (0.4)
呼吸器、胸郭および縦隔障害	2 (3.0)	3 (4.4)	1 (1.5)	2 (2.6)	8 (2.9)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
喘息	0	0	1 (1.5)	0	1 (0.4)
発声障害	0	2 (2.9)	0	0	2 (0.7)
呼吸困難	1 (1.5)	0	0	1 (1.3)	2 (0.7)
鼻閉	0	1 (1.5)	0	0	1 (0.4)
口腔咽頭痛	0	0	0	1 (1.3)	1 (0.4)
湿性咳嗽	1 (1.5)	0	0	0	1 (0.4)
皮膚および皮下組織障害	5 (7.5)	1 (1.5)	9 (13.4)	8 (10.5)	23 (8.3)
ざ瘡	0	0	0	2 (2.6)	2 (0.7)
脱毛症	2 (3.0)	0	0	0	2 (0.7)
皮膚炎	0	0	0	1 (1.3)	1 (0.4)
ざ瘡様皮膚炎	0	0	1 (1.5)	0	1 (0.4)
皮膚乾燥	0	0	1 (1.5)	1 (1.3)	2 (0.7)
湿疹	0	0	3 (4.5)	0	3 (1.1)
紅斑	0	0	0	1 (1.3)	1 (0.4)
結節性紅斑	0	0	1 (1.5)	0	1 (0.4)
手皮膚炎	1 (1.5)	0	0	0	1 (0.4)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
皮膚および皮下組織障害 (Cont.)					
多汗症	0	0	0	1 (1.3)	1 (0.4)
色素沈着障害	0	0	1 (1.5)	0	1 (0.4)
そう痒症	0	0	1 (1.5)	0	1 (0.4)
壊疽性膿皮症	1 (1.5)	0	0	0	1 (0.4)
発疹	1 (1.5)	0	1 (1.5)	2 (2.6)	4 (1.4)
紅斑性皮疹	0	0	0	1 (1.3)	1 (0.4)
そう痒性皮疹	1 (1.5)	0	0	1 (1.3)	2 (0.7)
酒さ	0	0	0	1 (1.3)	1 (0.4)
皮膚亀裂	0	0	1 (1.5)	0	1 (0.4)
皮膚線条	0	0	0	1 (1.3)	1 (0.4)
蕁麻疹	0	1 (1.5)	1 (1.5)	0	2 (0.7)
血管障害	0	0	0	1 (1.3)	1 (0.4)
表在性血栓性静脈炎	0	0	0	1 (1.3)	1 (0.4)

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]

表7

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RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 11

TABLE 14.3__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
Any adverse event	39 (21.0)	84 (22.5)	69 (18.5)	153 (20.5)
血液およびリンパ系障害	3 (1.6)	6 (1.6)	2 (0.5)	8 (1.1)
貧血	1 (0.5)	4 (1.1)	1 (0.3)	5 (0.7)
好酸球増加症	1 (0.5)	0	0	0
白血球減少症	1 (0.5)	1 (0.3)	0	1 (0.1)
リンパ球減少症	0	1 (0.3)	1 (0.3)	2 (0.3)
小球性貧血	0	1 (0.3)	0	1 (0.1)
心臓障害	0	0	2 (0.5)	2 (0.3)
不整脈	0	0	1 (0.3)	1 (0.1)
動悸	0	0	1 (0.3)	1 (0.1)
耳および迷路障害	2 (1.1)	0	0	0
回転性めまい	2 (1.1)	0	0	0
内分泌障害	0	1 (0.3)	0	1 (0.1)
甲状腺腫瘤	0	1 (0.3)	0	1 (0.1)
眼障害	0	4 (1.1)	0	4 (0.5)
ドライアイ	0	1 (0.3)	0	1 (0.1)

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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
眼障害 (Cont.)				
眼そう痒症	0	3 (0.8)	0	3 (0.4)
胃腸障害	8 (4.3)	13 (3.5)	16 (4.3)	29 (3.9)
腹部膨満	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)
腹痛	1 (0.5)	1 (0.3)	3 (0.8)	4 (0.5)
痔瘻	0	1 (0.3)	0	1 (0.1)
肛門狭窄	0	0	1 (0.3)	1 (0.1)
口唇炎	0	0	1 (0.3)	1 (0.1)
便秘	0	3 (0.8)	0	3 (0.4)
クローン病	4 (2.2)	0	1 (0.3)	1 (0.1)
下痢	0	1 (0.3)	1 (0.3)	2 (0.3)
消化不良	1 (0.5)	0	0	0
鼓腸	0	2 (0.5)	2 (0.5)	4 (0.5)
口の感覚鈍麻	0	0	1 (0.3)	1 (0.1)
回腸狭窄	0	0	1 (0.3)	1 (0.1)
大腸狭窄	0	1 (0.3)	0	1 (0.1)
悪心	3 (1.6)	5 (1.3)	6 (1.6)	11 (1.5)

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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
胃腸障害 (Cont.)				
嚥下痛	0	0	1 (0.3)	1 (0.1)
口の錯感覚	0	1 (0.3)	0	1 (0.1)
直腸分泌物	0	1 (0.3)	0	1 (0.1)
直腸出血	1 (0.5)	0	1 (0.3)	1 (0.1)
小腸閉塞	0	0	1 (0.3)	1 (0.1)
嘔吐	0	1 (0.3)	0	1 (0.1)
一般・全身障害および投与部位の状態	1 (0.5)	16 (4.3)	18 (4.8)	34 (4.6)
無力症	0	1 (0.3)	0	1 (0.1)
胸部不快感	0	0	1 (0.3)	1 (0.1)
胸痛	0	0	1 (0.3)	1 (0.1)
疲労	0	11 (2.9)	9 (2.4)	20 (2.7)
インフルエンザ様疾患	0	0	1 (0.3)	1 (0.1)
注射部位紅斑	0	0	1 (0.3)	1 (0.1)
注射部位知覚異常	0	0	1 (0.3)	1 (0.1)
倦怠感	0	1 (0.3)	0	1 (0.1)
末梢性浮腫	0	1 (0.3)	0	1 (0.1)

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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
疼痛	0	1 (0.3)	0	1 (0.1)
発熱	1 (0.5)	1 (0.3)	4 (1.1)	5 (0.7)
腫脹	0	0	1 (0.3)	1 (0.1)
全身性炎症反応症候群	0	0	1 (0.3)	1 (0.1)
肝胆道系障害	1 (0.5)	4 (1.1)	2 (0.5)	6 (0.8)
薬物性肝障害	0	1 (0.3)	0	1 (0.1)
肝機能異常	1 (0.5)	3 (0.8)	1 (0.3)	4 (0.5)
肝毒性	0	0	1 (0.3)	1 (0.1)
感染症および寄生虫症	13 (7.0)	20 (5.4)	16 (4.3)	36 (4.8)
肛門膿瘍	0	2 (0.5)	0	2 (0.3)
痔瘻感染	1 (0.5)	0	0	0
細菌感染	0	0	1 (0.3)	1 (0.1)
細菌性膣症	0	1 (0.3)	1 (0.3)	2 (0.3)
気管支炎	0	0	2 (0.5)	2 (0.3)
結膜炎	1 (0.5)	0	0	0
医療機器関連敗血症	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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
感染症および寄生虫症 (Cont.)				
耳感染	0	0	1 (0.3)	1 (0.1)
胃腸炎	1 (0.5)	0	0	0
真菌性性器感染	0	1 (0.3)	0	1 (0.1)
単純ヘルペス	0	1 (0.3)	0	1 (0.1)
ヘルペスウイルス感染	0	0	1 (0.3)	1 (0.1)
帯状疱疹	0	2 (0.5)	1 (0.3)	3 (0.4)
インフルエンザ	0	1 (0.3)	1 (0.3)	2 (0.3)
喉頭炎	0	1 (0.3)	0	1 (0.1)
下気道感染	0	1 (0.3)	0	1 (0.1)
上咽頭炎	2 (1.1)	9 (2.4)	5 (1.3)	14 (1.9)
咽頭炎	0	1 (0.3)	0	1 (0.1)
肺炎	2 (1.1)	0	0	0
腎盂腎炎	1 (0.5)	0	0	0
鼻炎	1 (0.5)	0	1 (0.3)	1 (0.1)
副鼻腔炎	1 (0.5)	0	0	0
上気道感染	1 (0.5)	0	3 (0.8)	3 (0.4)

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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
感染症および寄生虫症 (Cont.)				
ウイルス感染	1 (0.5)	1 (0.3)	2 (0.5)	3 (0.4)
ウイルス性咽頭炎	1 (0.5)	0	0	0
ウイルス性上気道感染	1 (0.5)	0	0	0
女性外陰部蜂巣炎	1 (0.5)	0	0	0
外陰腟真菌感染	0	0	1 (0.3)	1 (0.1)
傷害、中毒および処置合併症	2 (1.1)	1 (0.3)	1 (0.3)	2 (0.3)
注入に伴う反応	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)
関節脱臼	1 (0.5)	0	0	0
臨床検査	2 (1.1)	6 (1.6)	9 (2.4)	15 (2.0)
アラニンアミノトランスフェラーゼ増加	0	0	2 (0.5)	2 (0.3)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (0.3)	1 (0.1)
血中リン減少	0	1 (0.3)	0	1 (0.1)
体温上昇	0	0	2 (0.5)	2 (0.3)
γ－グルタミルトランスフェラーゼ増加	0	1 (0.3)	0	1 (0.1)
肝酵素上昇	1 (0.5)	0	0	0
肝機能検査異常	0	1 (0.3)	0	1 (0.1)

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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
臨床検査 (Cont.)				
低比重リポ蛋白減少	0	0	1 (0.3)	1 (0.1)
リンパ球数減少	0	2 (0.5)	1 (0.3)	3 (0.4)
トランスアミナーゼ上昇	0	0	1 (0.3)	1 (0.1)
体重増加	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)
白血球数減少	0	0	1 (0.3)	1 (0.1)
代謝および栄養障害	1 (0.5)	1 (0.3)	0	1 (0.1)
食欲減退	0	1 (0.3)	0	1 (0.1)
電解質失調	1 (0.5)	0	0	0
低アルブミン血症	1 (0.5)	0	0	0
筋骨格系および結合組織障害	5 (2.7)	9 (2.4)	7 (1.9)	16 (2.1)
関節痛	3 (1.6)	4 (1.1)	5 (1.3)	9 (1.2)
関節障害	0	1 (0.3)	0	1 (0.1)
背部痛	0	2 (0.5)	0	2 (0.3)
瘻孔	0	0	1 (0.3)	1 (0.1)
筋痙縮	2 (1.1)	0	0	0
筋骨格系胸痛	0	1 (0.3)	0	1 (0.1)

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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
筋骨格系および結合組織障害 (Cont.)				
筋肉痛	0	1 (0.3)	1 (0.3)	2 (0.3)
頚部痛	0	0	1 (0.3)	1 (0.1)
骨減少症	0	1 (0.3)	0	1 (0.1)
四肢痛	0	1 (0.3)	1 (0.3)	2 (0.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.5)	1 (0.3)	0	1 (0.1)
皮膚乳頭腫	1 (0.5)	1 (0.3)	0	1 (0.1)
神経系障害	5 (2.7)	16 (4.3)	14 (3.8)	30 (4.0)
浮動性めまい	1 (0.5)	2 (0.5)	4 (1.1)	6 (0.8)
味覚不全	1 (0.5)	1 (0.3)	0	1 (0.1)
顔面麻痺	0	1 (0.3)	0	1 (0.1)
頭痛	3 (1.6)	8 (2.1)	8 (2.2)	16 (2.1)
感覚鈍麻	0	0	2 (0.5)	2 (0.3)
嗜眠	0	2 (0.5)	1 (0.3)	3 (0.4)
片頭痛	0	1 (0.3)	0	1 (0.1)
錯感覚	0	1 (0.3)	0	1 (0.1)
振戦	0	1 (0.3)	0	1 (0.1)

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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
精神障害	1 (0.5)	2 (0.5)	1 (0.3)	3 (0.4)
感情障害	0	1 (0.3)	0	1 (0.1)
不安	0	0	1 (0.3)	1 (0.1)
失見当識	1 (0.5)	0	0	0
不眠症	0	1 (0.3)	0	1 (0.1)
腎および尿路障害	1 (0.5)	0	1 (0.3)	1 (0.1)
膀胱刺激症状	0	0	1 (0.3)	1 (0.1)
腎結石症	1 (0.5)	0	0	0
呼吸器、胸郭および縦隔障害	4 (2.2)	3 (0.8)	2 (0.5)	5 (0.7)
失声症	0	0	1 (0.3)	1 (0.1)
咳嗽	2 (1.1)	0	0	0
呼吸困難	0	0	1 (0.3)	1 (0.1)
鼻出血	0	1 (0.3)	0	1 (0.1)
しゃっくり	0	1 (0.3)	0	1 (0.1)
鼻潰瘍	0	1 (0.3)	0	1 (0.1)
口腔咽頭痛	3 (1.6)	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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
湿性咳嗽	0	1 (0.3)	1 (0.3)	2 (0.3)
皮膚および皮下組織障害	3 (1.6)	20 (5.4)	16 (4.3)	36 (4.8)
ざ瘡	0	1 (0.3)	2 (0.5)	3 (0.4)
脱毛症	0	6 (1.6)	1 (0.3)	7 (0.9)
水疱	0	1 (0.3)	0	1 (0.1)
皮膚症	0	0	1 (0.3)	1 (0.1)
皮膚乾燥	0	1 (0.3)	0	1 (0.1)
湿疹	1 (0.5)	1 (0.3)	2 (0.5)	3 (0.4)
紅斑	1 (0.5)	0	3 (0.8)	3 (0.4)
結節性紅斑	0	0	1 (0.3)	1 (0.1)
多汗症	0	1 (0.3)	0	1 (0.1)
間擦疹	0	0	1 (0.3)	1 (0.1)
寝汗	0	1 (0.3)	0	1 (0.1)
爪破損	0	1 (0.3)	0	1 (0.1)
丘疹	0	0	1 (0.3)	1 (0.1)
光線過敏性反応	0	0	2 (0.5)	2 (0.3)

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__1.1.4.4

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
皮膚および皮下組織障害 (Cont.)				
そう痒症	1 (0.5)	1 (0.3)	3 (0.8)	4 (0.5)
発疹	0	7 (1.9)	0	7 (0.9)
斑状丘疹状皮疹	0	0	1 (0.3)	1 (0.1)
そう痒性皮疹	1 (0.5)	0	0	0
脂漏性皮膚炎	0	1 (0.3)	1 (0.3)	2 (0.3)
蕁麻疹	1 (0.5)	0	0	0
血管障害	1 (0.5)	2 (0.5)	2 (0.5)	4 (0.5)
潮紅	0	1 (0.3)	0	1 (0.1)
血腫	1 (0.5)	0	0	0
ほてり	0	0	1 (0.3)	1 (0.1)
高血圧	0	1 (0.3)	0	1 (0.1)
収縮期高血圧	0	0	1 (0.3)	1 (0.1)

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] 00:59 <[redacted]>
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - CLINICAL/STATISTICAL

TABLE 14.3__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug by System Organ Class and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
Any adverse event	9 (13.4)	15 (22.1)	9 (13.4)	17 (22.4)	50 (18.0)
血液およびリンパ系障害	0	3 (4.4)	0	0	3 (1.1)
貧血	0	1 (1.5)	0	0	1 (0.4)
リンパ球減少症	0	2 (2.9)	0	0	2 (0.7)
心臓障害	1 (1.5)	0	0	0	1 (0.4)
動悸	1 (1.5)	0	0	0	1 (0.4)
胃腸障害	0	0	0	2 (2.6)	2 (0.7)
悪心	0	0	0	2 (2.6)	2 (0.7)
一般・全身障害および投与部位の状態	0	3 (4.4)	1 (1.5)	4 (5.3)	8 (2.9)
無力症	0	0	0	1 (1.3)	1 (0.4)
疲労	0	1 (1.5)	0	1 (1.3)	2 (0.7)
インフルエンザ様疾患	0	1 (1.5)	0	0	1 (0.4)
注射部位紅斑	0	0	0	1 (1.3)	1 (0.4)
注射部位疼痛	0	0	1 (1.5)	0	1 (0.4)
注射部位腫脹	0	1 (1.5)	0	0	1 (0.4)
注射部位熱感	0	0	0	1 (1.3)	1 (0.4)

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__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug by System Organ Class and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
免疫系障害	0	1 (1.5)	0	0	1 (0.4)
過敏症	0	1 (1.5)	0	0	1 (0.4)
感染症および寄生虫症	3 (4.5)	9 (13.2)	3 (4.5)	3 (3.9)	18 (6.5)
気管支炎	1 (1.5)	2 (2.9)	0	0	3 (1.1)
エンテロバクター感染	0	0	1 (1.5)	0	1 (0.4)
大腸菌性尿路感染	0	1 (1.5)	0	0	1 (0.4)
毛包炎	0	0	1 (1.5)	0	1 (0.4)
胃腸炎	1 (1.5)	0	0	0	1 (0.4)
ノロウイルス性胃腸炎	0	0	0	1 (1.3)	1 (0.4)
単純ヘルペス	1 (1.5)	0	0	0	1 (0.4)
帯状疱疹	0	1 (1.5)	0	0	1 (0.4)
インフルエンザ	0	3 (4.4)	0	0	3 (1.1)
上咽頭炎	0	1 (1.5)	0	0	1 (0.4)
中耳炎	0	1 (1.5)	0	0	1 (0.4)
細菌性咽頭炎	0	1 (1.5)	0	0	1 (0.4)
ウイルス性気道感染	0	0	0	1 (1.3)	1 (0.4)

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__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug by System Organ Class and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
感染症および寄生虫症 (Cont.)					
鼻炎	0	0	1 (1.5)	1 (1.3)	2 (0.7)
ブドウ球菌皮膚感染	1 (1.5)	0	0	0	1 (0.4)
足部白癬	0	0	1 (1.5)	0	1 (0.4)
気管気管支炎	0	0	0	1 (1.3)	1 (0.4)
上気道感染	1 (1.5)	1 (1.5)	0	0	2 (0.7)
膿創	0	0	1 (1.5)	0	1 (0.4)
臨床検査	2 (3.0)	1 (1.5)	2 (3.0)	0	5 (1.8)
アラニンアミノトランスフェラーゼ増加	0	0	1 (1.5)	0	1 (0.4)
血中アルカリホスファターゼ増加	0	0	1 (1.5)	0	1 (0.4)
血中クレアチンホスホキナーゼ増加	1 (1.5)	0	0	0	1 (0.4)
γ－グルタミルトランスフェラーゼ増加	0	0	1 (1.5)	0	1 (0.4)
リンパ球数減少	0	1 (1.5)	0	0	1 (0.4)
好中球百分率増加	0	0	1 (1.5)	0	1 (0.4)
血小板数減少	1 (1.5)	0	0	0	1 (0.4)
代謝および栄養障害	0	0	1 (1.5)	1 (1.3)	2 (0.7)
高トリグリセリド血症	0	0	1 (1.5)	1 (1.3)	2 (0.7)

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__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug by System Organ Class and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
筋骨格系および結合組織障害	0	0	2 (3.0)	4 (5.3)	6 (2.2)
関節痛	0	0	1 (1.5)	3 (3.9)	4 (1.4)
関節障害	0	0	0	1 (1.3)	1 (0.4)
筋肉痛	0	0	1 (1.5)	1 (1.3)	2 (0.7)
仙腸骨炎	0	0	0	1 (1.3)	1 (0.4)
神経系障害	2 (3.0)	1 (1.5)	0	5 (6.6)	8 (2.9)
浮動性めまい	0	0	0	2 (2.6)	2 (0.7)
頭痛	0	1 (1.5)	0	3 (3.9)	4 (1.4)
片頭痛	1 (1.5)	0	0	0	1 (0.4)
味覚障害	1 (1.5)	0	0	0	1 (0.4)
呼吸器、胸郭および縦隔障害	1 (1.5)	2 (2.9)	0	0	3 (1.1)
発声障害	0	2 (2.9)	0	0	2 (0.7)
湿性咳嗽	1 (1.5)	0	0	0	1 (0.4)
皮膚および皮下組織障害	2 (3.0)	1 (1.5)	4 (6.0)	3 (3.9)	10 (3.6)
脱毛症	1 (1.5)	0	0	0	1 (0.4)
ざ瘡様皮膚炎	0	0	1 (1.5)	0	1 (0.4)

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__1.2.4.2

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility
of Being Related to Study Drug by System Organ Class and Preferred Term during the Induction Period 2
(SA2 Population)

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
皮膚および皮下組織障害 (Cont.)					
皮膚乾燥	0	0	1 (1.5)	0	1 (0.4)
湿疹	0	0	1 (1.5)	0	1 (0.4)
紅斑	0	0	0	1 (1.3)	1 (0.4)
手皮膚炎	1 (1.5)	0	0	0	1 (0.4)
発疹	0	0	1 (1.5)	1 (1.3)	2 (0.7)
紅斑性皮疹	0	0	0	1 (1.3)	1 (0.4)
そう痒性皮疹	1 (1.5)	0	0	0	1 (0.4)
蕁麻疹	0	1 (1.5)	0	0	1 (0.4)
血管障害	0	0	0	1 (1.3)	1 (0.4)
表在性血栓性静脈炎	0	0	0	1 (1.3)	1 (0.4)

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]

表9

[redacted]20[redacted] 00:59 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.5.3

Subjects with Treatment-Emergent Severe 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
Any adverse event	18 (9.7)	22 (5.9)	18 (4.8)	40 (5.4)
血液およびリンパ系障害	1 (0.5)	1 (0.3)	2 (0.5)	3 (0.4)
貧血	1 (0.5)	1 (0.3)	2 (0.5)	3 (0.4)
心臓障害	0	1 (0.3)	0	1 (0.1)
心室性頻脈	0	1 (0.3)	0	1 (0.1)
胃腸障害	12 (6.5)	10 (2.7)	6 (1.6)	16 (2.1)
腹部膨満	0	0	1 (0.3)	1 (0.1)
腹痛	3 (1.6)	0	1 (0.3)	1 (0.1)
下腹部痛	0	1 (0.3)	0	1 (0.1)
肛門直腸障害	1 (0.5)	0	0	0
大腸炎	1 (0.5)	0	0	0
クローン病	8 (4.3)	3 (0.8)	3 (0.8)	6 (0.8)
下痢	0	1 (0.3)	0	1 (0.1)
胃腸の炎症	1 (0.5)	0	0	0
消化管壊死	1 (0.5)	0	0	0
回腸穿孔	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__1.1.5.3

Subjects with Treatment-Emergent Severe 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
胃腸障害 (Cont.)				
回腸狭窄	0	0	1 (0.3)	1 (0.1)
イレウス	0	2 (0.5)	0	2 (0.3)
腸閉塞	1 (0.5)	1 (0.3)	0	1 (0.1)
腸管狭窄	1 (0.5)	0	0	0
大腸穿孔	0	1 (0.3)	1 (0.3)	2 (0.3)
小腸閉塞	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)
歯痛	0	1 (0.3)	0	1 (0.1)
嘔吐	0	1 (0.3)	0	1 (0.1)
一般・全身障害および投与部位の状態	1 (0.5)	0	2 (0.5)	2 (0.3)
疲労	1 (0.5)	0	1 (0.3)	1 (0.1)
全身性炎症反応症候群	0	0	1 (0.3)	1 (0.1)
肝胆道系障害	0	2 (0.5)	1 (0.3)	3 (0.4)
薬物性肝障害	0	1 (0.3)	0	1 (0.1)
肝機能異常	0	1 (0.3)	0	1 (0.1)
肝毒性	0	0	1 (0.3)	1 (0.1)
感染症および寄生虫症	8 (4.3)	2 (0.5)	3 (0.8)	5 (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__1.1.5.3

Subjects with Treatment-Emergent Severe 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
感染症および寄生虫症 (Cont.)				
腹壁膿瘍	1 (0.5)	0	0	0
腸管膿瘍	1 (0.5)	0	0	0
肛門膿瘍	1 (0.5)	0	0	0
胃腸炎	0	0	1 (0.3)	1 (0.1)
下気道感染	0	1 (0.3)	0	1 (0.1)
肺炎	2 (1.1)	0	1 (0.3)	1 (0.1)
術後創感染	1 (0.5)	0	0	0
肺敗血症	1 (0.5)	0	0	0
腎盂腎炎	1 (0.5)	0	0	0
皮膚感染	0	0	1 (0.3)	1 (0.1)
扁桃炎	1 (0.5)	0	0	0
結核	0	1 (0.3)	0	1 (0.1)
尿路感染	0	0	1 (0.3)	1 (0.1)
女性外陰部蜂巣炎	1 (0.5)	0	0	0
傷害、中毒および処置合併症	1 (0.5)	1 (0.3)	0	1 (0.1)
転倒	0	1 (0.3)	0	1 (0.1)

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__1.1.5.3

Subjects with Treatment-Emergent Severe 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
傷害、中毒および処置合併症 (Cont.)				
前腕骨折	0	1 (0.3)	0	1 (0.1)
創離開	1 (0.5)	0	0	0
臨床検査	0	1 (0.3)	1 (0.3)	2 (0.3)
ヘモグロビン減少	0	0	1 (0.3)	1 (0.1)
リンパ球数減少	0	1 (0.3)	0	1 (0.1)
代謝および栄養障害	0	0	1 (0.3)	1 (0.1)
糖尿病	0	0	1 (0.3)	1 (0.1)
筋骨格系および結合組織障害	0	4 (1.1)	1 (0.3)	5 (0.7)
強直性脊椎炎	0	1 (0.3)	0	1 (0.1)
関節痛	0	1 (0.3)	0	1 (0.1)
関節炎	0	1 (0.3)	0	1 (0.1)
瘻孔	0	0	1 (0.3)	1 (0.1)
筋骨格痛	0	1 (0.3)	0	1 (0.1)
頚部痛	0	1 (0.3)	0	1 (0.1)
神経系障害	0	1 (0.3)	0	1 (0.1)
頭痛	0	1 (0.3)	0	1 (0.1)

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__1.1.5.3

Subjects with Treatment-Emergent Severe 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
腎および尿路障害	1 (0.5)	0	2 (0.5)	2 (0.3)
膀胱刺激症状	0	0	1 (0.3)	1 (0.1)
腎結石症	1 (0.5)	0	1 (0.3)	1 (0.1)
生殖系および乳房障害	1 (0.5)	0	0	0
子宮頚部上皮異形成	1 (0.5)	0	0	0
呼吸器、胸郭および縦隔障害	0	1 (0.3)	1 (0.3)	2 (0.3)
喘息	0	1 (0.3)	0	1 (0.1)
肺塞栓症	0	0	1 (0.3)	1 (0.1)
外科および内科処置	0	1 (0.3)	0	1 (0.1)
人工流産	0	1 (0.3)	0	1 (0.1)
血管障害	0	1 (0.3)	1 (0.3)	2 (0.3)
深部静脈血栓症	0	0	1 (0.3)	1 (0.1)
高血圧	0	1 (0.3)	0	1 (0.1)

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] 00:59 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - CLINICAL/STATISTICAL

TABLE 14.3__1.2.5.1

Subjects with Treatment-Emergent Severe 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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
Any adverse event	2 (3.0)	4 (5.9)	3 (4.5)	5 (6.6)	14 (5.0)
眼障害	0	0	0	1 (1.3)	1 (0.4)
網膜障害	0	0	0	1 (1.3)	1 (0.4)
胃腸障害	1 (1.5)	2 (2.9)	2 (3.0)	2 (2.6)	7 (2.5)
腹部ヘルニア	0	0	1 (1.5)	0	1 (0.4)
腹痛	1 (1.5)	0	0	0	1 (0.4)
クローン病	1 (1.5)	0	0	0	1 (0.4)
消化管壊死	0	0	1 (1.5)	0	1 (0.4)
腸管虚血	0	0	1 (1.5)	0	1 (0.4)
腸閉塞	1 (1.5)	1 (1.5)	0	1 (1.3)	3 (1.1)
大腸穿孔	0	1 (1.5)	0	0	1 (0.4)
小腸閉塞	0	0	1 (1.5)	0	1 (0.4)
亜イレウス	0	0	0	1 (1.3)	1 (0.4)
嘔吐	0	0	1 (1.5)	0	1 (0.4)
感染症および寄生虫症	0	1 (1.5)	0	0	1 (0.4)
腹膜炎	0	1 (1.5)	0	0	1 (0.4)

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__1.2.5.1

Subjects with Treatment-Emergent Severe 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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
代謝および栄養障害	0	0	0	1 (1.3)	1 (0.4)
高トリグリセリド血症	0	0	0	1 (1.3)	1 (0.4)
筋骨格系および結合組織障害	0	1 (1.5)	0	0	1 (0.4)
背部痛	0	1 (1.5)	0	0	1 (0.4)
精神障害	0	1 (1.5)	1 (1.5)	1 (1.3)	3 (1.1)
不眠症	0	0	0	1 (1.3)	1 (0.4)
精神障害	0	1 (1.5)	0	0	1 (0.4)
強迫性障害	0	0	1 (1.5)	0	1 (0.4)
腎および尿路障害	1 (1.5)	0	1 (1.5)	0	2 (0.7)
尿路結石	1 (1.5)	0	0	0	1 (0.4)
尿管結石症	0	0	1 (1.5)	0	1 (0.4)

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]

表11

[redacted]20[redacted] 00:59 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - 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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
Any adverse event	2 (1.1)	0	0	0
胃腸障害	1 (0.5)	0	0	0
消化管壊死	1 (0.5)	0	0	0
回腸穿孔	1 (0.5)	0	0	0
腸管狭窄	1 (0.5)	0	0	0
感染症および寄生虫症	1 (0.5)	0	0	0
肺炎	1 (0.5)	0	0	0
肺敗血症	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]

表12

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
Any adverse event	28 (15.1)	27 (7.2)	14 (3.8)	41 (5.5)
血液およびリンパ系障害	1 (0.5)	0	1 (0.3)	1 (0.1)
貧血	1 (0.5)	0	1 (0.3)	1 (0.1)
心臓障害	0	1 (0.3)	0	1 (0.1)
心室性頻脈	0	1 (0.3)	0	1 (0.1)
胃腸障害	20 (10.8)	13 (3.5)	5 (1.3)	18 (2.4)
腹痛	2 (1.1)	0	0	0
大腸炎	1 (0.5)	0	0	0
クローン病	15 (8.1)	5 (1.3)	2 (0.5)	7 (0.9)
下痢	0	1 (0.3)	0	1 (0.1)
胃腸出血	0	1 (0.3)	0	1 (0.1)
胃腸の炎症	1 (0.5)	0	0	0
消化管壊死	1 (0.5)	0	0	0
回腸穿孔	1 (0.5)	0	0	0
回腸狭窄	0	0	1 (0.3)	1 (0.1)
イレウス	0	2 (0.5)	0	2 (0.3)

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__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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
胃腸障害 (Cont.)				
腸閉塞	2 (1.1)	1 (0.3)	0	1 (0.1)
腸管狭窄	2 (1.1)	0	0	0
大腸穿孔	0	1 (0.3)	1 (0.3)	2 (0.3)
悪心	0	1 (0.3)	0	1 (0.1)
急性膵炎	0	1 (0.3)	0	1 (0.1)
小腸閉塞	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)
末端回腸炎	0	0	1 (0.3)	1 (0.1)
嘔吐	1 (0.5)	1 (0.3)	0	1 (0.1)
一般・全身障害および投与部位の状態	1 (0.5)	0	1 (0.3)	1 (0.1)
無力症	1 (0.5)	0	0	0
全身性炎症反応症候群	0	0	1 (0.3)	1 (0.1)
肝胆道系障害	0	2 (0.5)	1 (0.3)	3 (0.4)
胆管結石	0	1 (0.3)	0	1 (0.1)
胆管炎	0	1 (0.3)	0	1 (0.1)
肝機能異常	0	1 (0.3)	0	1 (0.1)
肝障害	0	0	1 (0.3)	1 (0.1)

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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
免疫系障害	0	1 (0.3)	0	1 (0.1)
食物アレルギー	0	1 (0.3)	0	1 (0.1)
感染症および寄生虫症	7 (3.8)	3 (0.8)	2 (0.5)	5 (0.7)
腹壁膿瘍	1 (0.5)	0	0	0
腸管膿瘍	1 (0.5)	0	0	0
肛門膿瘍	1 (0.5)	0	0	0
虫垂炎	0	1 (0.3)	0	1 (0.1)
胃腸炎	1 (0.5)	0	0	0
レプトスピラ症	0	1 (0.3)	0	1 (0.1)
下気道感染	0	1 (0.3)	0	1 (0.1)
肺炎	1 (0.5)	0	1 (0.3)	1 (0.1)
肺敗血症	1 (0.5)	0	0	0
腎盂腎炎	1 (0.5)	0	0	0
扁桃炎	1 (0.5)	0	0	0
尿路感染	0	0	1 (0.3)	1 (0.1)
女性外陰部蜂巣炎	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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
傷害、中毒および処置合併症	0	1 (0.3)	0	1 (0.1)
転倒	0	1 (0.3)	0	1 (0.1)
前腕骨折	0	1 (0.3)	0	1 (0.1)
臨床検査	1 (0.5)	0	2 (0.5)	2 (0.3)
体温上昇	0	0	1 (0.3)	1 (0.1)
ヘモグロビン減少	0	0	1 (0.3)	1 (0.1)
体重減少	1 (0.5)	0	0	0
筋骨格系および結合組織障害	1 (0.5)	3 (0.8)	1 (0.3)	4 (0.5)
強直性脊椎炎	0	1 (0.3)	0	1 (0.1)
関節痛	0	1 (0.3)	0	1 (0.1)
線維筋痛	0	1 (0.3)	0	1 (0.1)
瘻孔	0	0	1 (0.3)	1 (0.1)
脊椎炎	1 (0.5)	0	0	0
神経系障害	2 (1.1)	0	0	0
浮動性めまい	1 (0.5)	0	0	0
失神	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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
腎および尿路障害	1 (0.5)	2 (0.5)	1 (0.3)	3 (0.4)
水腎症	0	1 (0.3)	0	1 (0.1)
腎結石症	1 (0.5)	0	1 (0.3)	1 (0.1)
尿管結石症	0	2 (0.5)	0	2 (0.3)
呼吸器、胸郭および縦隔障害	0	1 (0.3)	1 (0.3)	2 (0.3)
喘息	0	1 (0.3)	0	1 (0.1)
肺塞栓症	0	0	1 (0.3)	1 (0.1)
皮膚および皮下組織障害	0	1 (0.3)	0	1 (0.1)
発疹	0	1 (0.3)	0	1 (0.1)
外科および内科処置	0	1 (0.3)	0	1 (0.1)
人工流産	0	1 (0.3)	0	1 (0.1)
血管障害	0	1 (0.3)	1 (0.3)	2 (0.3)
深部静脈血栓症	0	0	1 (0.3)	1 (0.1)
高血圧	0	1 (0.3)	0	1 (0.1)

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13

[redacted]20[redacted] 00:59 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - 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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
Any adverse event	3 (4.5)	3 (4.4)	4 (6.0)	4 (5.3)	14 (5.0)
眼障害	0	0	0	1 (1.3)	1 (0.4)
網膜障害	0	0	0	1 (1.3)	1 (0.4)
胃腸障害	2 (3.0)	2 (2.9)	2 (3.0)	2 (2.6)	8 (2.9)
腹部ヘルニア	0	0	1 (1.5)	0	1 (0.4)
クローン病	1 (1.5)	0	0	0	1 (0.4)
消化管壊死	0	0	1 (1.5)	0	1 (0.4)
腸管虚血	0	0	1 (1.5)	0	1 (0.4)
腸閉塞	1 (1.5)	1 (1.5)	0	1 (1.3)	3 (1.1)
大腸穿孔	0	1 (1.5)	0	0	1 (0.4)
小腸閉塞	0	0	1 (1.5)	0	1 (0.4)
亜イレウス	0	0	0	1 (1.3)	1 (0.4)
嘔吐	0	0	1 (1.5)	0	1 (0.4)
肝胆道系障害	0	0	1 (1.5)	0	1 (0.4)
急性胆嚢炎	0	0	1 (1.5)	0	1 (0.4)
感染症および寄生虫症	0	1 (1.5)	0	1 (1.3)	2 (0.7)

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=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
感染症および寄生虫症 (Cont.)					
ノロウイルス性胃腸炎	0	0	0	1 (1.3)	1 (0.4)
腹膜炎	0	1 (1.5)	0	0	1 (0.4)
精神障害	0	1 (1.5)	1 (1.5)	0	2 (0.7)
精神障害	0	1 (1.5)	0	0	1 (0.4)
強迫性障害	0	0	1 (1.5)	0	1 (0.4)
腎および尿路障害	1 (1.5)	0	1 (1.5)	0	2 (0.7)
尿路結石	1 (1.5)	0	0	0	1 (0.4)
尿管結石症	0	0	1 (1.5)	0	1 (0.4)

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]

表14

[redacted]20[redacted] 00:59 <[redacted] >
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - CLINICAL/STATISTICAL

TABLE 14.3__2.1.3.4

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
Any adverse event	14 (7.5)	9 (2.4)	7 (1.9)	16 (2.1)
胃腸障害	9 (4.8)	2 (0.5)	3 (0.8)	5 (0.7)
クローン病	7 (3.8)	2 (0.5)	2 (0.5)	4 (0.5)
下痢	1 (0.5)	0	0	0
消化管壊死	1 (0.5)	0	0	0
回腸穿孔	1 (0.5)	0	0	0
腸管狭窄	1 (0.5)	0	0	0
小腸閉塞	1 (0.5)	0	1 (0.3)	1 (0.1)
嘔吐	1 (0.5)	0	0	0
一般・全身障害および投与部位の状態	1 (0.5)	1 (0.3)	1 (0.3)	2 (0.3)
発熱	1 (0.5)	1 (0.3)	0	1 (0.1)
全身性炎症反応症候群	0	0	1 (0.3)	1 (0.1)
肝胆道系障害	0	1 (0.3)	0	1 (0.1)
肝機能異常	0	1 (0.3)	0	1 (0.1)
感染症および寄生虫症	4 (2.2)	0	0	0
腹部膿瘍	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__2.1.3.4

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
感染症および寄生虫症 (Cont.)				
肛門膿瘍	1 (0.5)	0	0	0
肺炎	2 (1.1)	0	0	0
肺敗血症	1 (0.5)	0	0	0
傷害、中毒および処置合併症	0	1 (0.3)	1 (0.3)	2 (0.3)
注入に伴う反応	0	1 (0.3)	1 (0.3)	2 (0.3)
臨床検査	0	1 (0.3)	1 (0.3)	2 (0.3)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (0.3)	0	1 (0.1)
ホルモン値異常	0	0	1 (0.3)	1 (0.1)
筋骨格系および結合組織障害	0	1 (0.3)	1 (0.3)	2 (0.3)
関節痛	0	1 (0.3)	0	1 (0.1)
瘻孔	0	0	1 (0.3)	1 (0.1)
精神障害	1 (0.5)	0	0	0
失見当識	1 (0.5)	0	0	0
皮膚および皮下組織障害	1 (0.5)	2 (0.5)	1 (0.3)	3 (0.4)
水疱	0	1 (0.3)	0	1 (0.1)
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__2.1.3.4

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=186) n (%)	Risankizumab 600 mg IV (N=373) n (%)	Risankizumab 1200 mg IV (N=372) n (%)	Risankizumab Total (N=745) n (%)
皮膚および皮下組織障害 (Cont.)				
発疹	0	1 (0.3)	0	1 (0.1)
斑状丘疹状皮疹	0	0	1 (0.3)	1 (0.1)
そう痒性皮疹	1 (0.5)	0	0	0
蕁麻疹	1 (0.5)	0	0	0
外科および内科処置	0	1 (0.3)	0	1 (0.1)
人工流産	0	1 (0.3)	0	1 (0.1)

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15

[redacted]20[redacted] 00:59 <[redacted]>
RISANKIZUMAB (CROHN'S DISEASE)
STUDY M16-006
R&D/20/1216 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.2.3.1

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

System Organ Class MedDRA 23.1 Preferred Term	Risankizumab 180 mg SC (N=67) n (%)	Risankizumab 360 mg SC (N=68) n (%)	Risankizumab 1200 mg IV (N=67) n (%)	Placebo IV/ Risankizumab 1200 mg IV (N=76) n (%)	Total (N=278) n (%)
Any adverse event	0	1 (1.5)	0	0	1 (0.4)
胃腸障害	0	1 (1.5)	0	0	1 (0.4)
腸閉塞	0	1 (1.5)	0	0	1 (0.4)

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]

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肺炎		X		
女性外陰部蜂巣炎	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: ECZEMA	19[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
ASTHMA	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: BILETERAL SCLERA ERYTHEMA	20[redacted]
OTHER: CROHN'S DISEASE	20[redacted]
OTHER: IRON DEFICIENCY ANEMIA	20[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
OTHER: HEADACHES	20[redacted]
OTHER: BENIGN LUNG NODULE	20[redacted]
OTHER: FLAGYL ALLERGY	20[redacted]
OTHER: LUNG BIOPSY	20[redacted]
OTHER: RIGHT BUTTOCK ABSCESS	20[redacted]
OTHER: RIGHT THIGH ABSCESS	20[redacted]
OTHER: VANCOMYCIN ALLERGY	20[redacted]
OTHER: VITAMIN D DEFICIENCY	20[redacted]
OTHER: THROMBOCYTOSIS	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: ANAL FISTULA	20[redacted]
OTHER: VITAMIN B12 DEFICIENCY	20[redacted]
OTHER: ORAL APHTHOUS ULCERS	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: FISTULOTOMY	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: INCISION AND DRAINAGE OF ANAL FISTULA	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: PLACEMENTS OF SETONS	20[redacted]
ENDOSCOPY (SCREENING): BIOPSY	20[redacted]

ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY 20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
DIHYDROXYALUMINUM SODIUM CARBONATE	4 OTHER: TABS	PRN	Y-M: 20[redacted]
CYPROHEPTADINE	4 mg	QD	Y-M: 20[redacted]
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y-M: 20[redacted]
DALIMUMAB	80 mg	OTHER: EVERY 2 WEEKS	Y-M: 20[redacted]
METHOTREXATE	12.5 mg	OTHER: WEEKLY	Y-M: 20[redacted]
INFLIXIMAB	200 mg	OTHER: WEEKS 0, 2, 6	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	500 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
TRAZODONE	50 mg	OTHER: Q HS	Y-M: 20[redacted]
USTEKINUMAB	260 mg	OTHER: ONCE	Y-M: 20[redacted]
USTEKINUMAB	90 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
CYANOCOBALAMIN	1000 OTHER: MCG	OTHER: Q MONTHLY	Y-M: 20[redacted]
MESALAZINE	60 mL	QD	Y-M: 20[redacted] / -256
FENTANYL	125 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / -35
MIDAZOLAM	6 mg	OTHER: ONCE	Y-M: 20[redacted] / -35
PROMETHAZINE	25 mg	OTHER: ONCE	Y-M: 20[redacted] / -35
AUGMENTIN	500 mg	BID	Y-M: 20[redacted] / -30

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
DIHYDROXYALUMINUM SODIUM CARBONATE	4 OTHER: TABS	PRN	Y-M: 20[redacted]	ONGOING
CYPROHEPTADINE	4 mg	QD	Y-M: 20[redacted]	ONGOING
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y-M: 20[redacted]	ONGOING
TRAZODONE	50 mg	OTHER: Q HS	Y-M: 20[redacted]	ONGOING
CYANOCOBALAMIN	1000 OTHER: MCG	OTHER: Q MONTHLY	Y-M: 20[redacted]	ONGOING
AUGMENTIN	500 mg	BID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 24
IBUPROFEN	800 mg	OTHER: OTHER	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21
PARACETAMOL	325 mg	OTHER: ONCE	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21
PIP/TAZO	3.375 g	OTHER: ONCE	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21
HYDROCODONE	5 mg	PRN	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 26
PARACETAMOL	325 mg	PRN	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 26
AMOXICILLIN	875 mg	BID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 32
BACTRIM	800 mg	BID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 32
DIPHENHYDRAMINE	50 mg	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 27
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 27
HYOSCINE	1 OTHER: PATCH	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 27
ONDANSETRON	4 mg	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 27
CLARITHROMYCIN	500 mg	BID	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 52

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

Event Description	RIGHT PERILABIAL CELLULITIS
Preferred term	女性外陰部蜂巣炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 7
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 21): Activated Partial Thromboplastin Time: 33 [25 - 36] sec; Alanine Aminotransferase: 8 [8 - 33] U/L; Albumin: 3.2 [3.3 - 4.6] g/dL; Alkaline Phosphatase: 90 [35 - 104] U/L; Aspartate Aminotransferase: 9 [11 - 32] U/L; Bilirubin: 0.4 [0.2 - 1.1] mg/dL; Bilirubin: NEGATIVE [Not reported - Not reported] Unit not reported; Blood Urea Nitrogen: 10 [7 - 21] mg/dL; C Reactive Protein: 5.4 [0 - 0.9] mg/dL; Calcium: 9.3 [8.9 - 10.2] mg/dL; Chloride: 103 [97 - 107] mmol/L; Creatinine: 0.67 [0.6 - 1.1] mg/dL; Ery. Mean Corpuscular Hemoglobin: 27.3 [26 - 32] pg; Ery. Mean Corpuscular Volume: 83 [79 - 98] fL; Erythrocytes: 4.54 [3.9 - 5.2] 10^12/L; Erythrocytes: LESS THAN 1 [0 - 3] /HPF; Glucose: 87 [74 - 99] mg/dL; Glucose: NEGATIVE [Not reported - Not reported] Unit not reported; Hematocrit: 37.5 [34 - 45] %; Hemoglobin: 12.4 [11.2 - 15.7] g/dL; Ketones: NEGATIVE [Not reported - Not reported] mg/dL; Leukocytes: 12.20 [3.7 - 10.3] 10^9/L; Leukocytes: 6-10 [0 - 5] /HPF; NPTST013-ANION GAP: 13 [6 - 16] mmol/L; NPTST032-BACTERIA: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST043-BLOOD CULTURE: NO GROWTH [Not reported - Not reported] Unit not reported; NPTST066-CO2: 24 [22 - 29] mmol/L; NPTST110-GFR: >60 [60 - Not reported] Unit not reported; NPTST140-HYALINE CASTS: 0-8 [0 - 8] Unit not reported; NPTST165-MAGNESIUM: 2.0 [1.9 - 2.4] mg/dL; NPTST167-MCHC: 33.1 [30.7 - 35.5] g/dL; NPTST178-MVP: 8.0 [8.8 - 12.5] fL; NPTST179-NITRITE: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST181-NRBC COUNT: 0.0 [0 - 0] %; NPTST195-PHOSPHORUS: 3.0 [2.5 - 4.5] mg/dL; NPTST201-PREGNANCY: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST215-RDW: 13.5 [11.5 - 14.5] %; NPTST252-SQUAMOUS EPITHELIAL CELLS: 6-10 [0 - 5] Unit not reported; NPTST267-UN/CREA RATIO: 15 [8 - 20] RATIO; NPTST273-URINE BLOOD: MODERATE [Not reported - Not reported] Unit not reported; NPTST274-URINE CLARIFY: CLOUDY [Not reported - Not reported] Unit not reported; NPTST275-URINE COLOR: YELLOW [Not reported - Not reported] Unit not reported; NPTST276-URINE CULTURE: CONTAMINATED URINE [Not reported - Not reported] Unit not reported; NPTST277-URINE LEUK ESTERASE: LARGE [Not reported - Not reported] Unit not reported; NPTST281-UROBILINOGEN: 0.2 [0.2 - 1] Unit not reported; NPTST282-VENOUS LACTIC ACID: 0.9 [0.5 - 2.2] mmol/L; Platelets: 670 [155 - 369] 10^9/L; Potassium: 4.0 [3.7 - 4.8] mmol/L; Protein: 7.5 [6.3 - 7.9] g/dL; Protein: NEGATIVE [Not reported - Not reported] Unit not reported; Prothrombin Intl. Normalized Ratio: 1.0 [0.9 - 1.1] Unit not reported; Prothrombin Time: 13.2 [12.3 - 14.8] sec; Sodium: 140 [136 - 145] mmol/L; Specific Gravity: 1.016 [1.001 - 1.03] Unit not reported; pH: 6.5 [4.5 - 8] Unit not reported

Microbiology

Not reported

SAE Supplemental Procedure

Not reported

AE Stopped Rx Day	32 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	26 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	Not reported
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	RIGHT LUNG PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 39 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing
Not Applicable
Microbiology
Not Applicable
SAE Supplemental Procedure
Not Applicable

AE Stopped Rx Day	52 (22 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	Not Applicable
Discontinued Study Drug Due to the Event	YES
SAE Criteria	None

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

米国の治験責任医師からの報告。本被験者は2[redacted]歳女性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，右外陰部蜂巣炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，湿疹，喘息，両眼強膜の紅斑，クローン病，鉄欠乏性貧血，季節性アレルギー，腸切除，右殿部膿瘍，右大腿膿瘍，瘻孔切開，痔瘻，痔瘻の切除及びドレナージ，シートン留置，口腔アフタ性潰瘍，非喫煙者及び飲酒者（1 日 2 杯未満）であった。

投与 7 日後，被験者は右外陰部の蜂巣炎を発現した。投与 32 日後，右外陰部蜂巣炎は消失した。

投与 21 日後，被験者は外陰部の病変，並びに前日から続く生殖器痛及び排尿困難があり，救急科（ED）を受診した。同日，被験者は入院した。身体的診察及び臨床検査が行われた。投与 21 日後，被験者は退院した。

右肺の肺炎（非重篤）により治験薬の投与が中止された。

投与された薬剤は，ゾシン，Bactrim，ヒドロコドン，アセトアミノフェン，イブプロフェン及びアモキシシリンであった。

The patient’s past medications include:

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

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

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

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

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

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

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

FLAGYL for UNKNOWN INDICATION

VANCOMYCIN for UNKNOWN INDICATION

Causality for RISANKIZUMAB (Blinded)

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1) Vulval cellulitis (10047752) (Vulval cellulitis (10047752)) [v.23.1] [10047752]

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 RIGHT PERILABIAL CELLULITIS

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing crohn's disease and history of multiple fistulas and abscesses.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 3.2 G/DL (normal 3.3 to 4.6)

[redacted] **20[redacted] APTT:** 33 SEC (normal 25 to 36)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 9 U/L (normal 11 to 32)

[redacted] 20[redacted] BLOOD CULTURES: No growth

[redacted] **20[redacted] CMP:** Not reported

[redacted] **20[redacted] GFR:** >60 mL/min/1.73 m2 (normal >60)

[redacted] 20[redacted] HEMOGRAM: Not reported

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 5.4 mg/dL (normal 0 to 0.9)

[redacted] 20[redacted] ILEOCOLONOSCOPY WITH 9 BIOPSIES (SCREENING): Not reported

[redacted] **20[redacted] MAGNESIUM:** 2.0 mg/dL (normal 1.9 to 2.4)

[redacted] **20[redacted] MVP:** 8.0 FL (normal 8.8 to 12.5)

[redacted] **20[redacted] PHOSPHORUS:** 3.0 mg/dL (normal 2.5 to 4.5)

[redacted] **20[redacted] PLATELET COUNT:** 670 k/uL (normal 155 to 369)

[redacted] 20[redacted] PREGNANCY TEST: Negative

[redacted] **20[redacted] PTI:** 13.2 SEC (normal 12.3 to 14.8)

[redacted] 20[redacted] URINE BACTERIA: Negative

[redacted] **20[redacted] URINE BLOOD:** Results: Moderate; Normal range: Negative

[redacted] **20[redacted] URINE CULTURES:** Contaminated urine, no growth

[redacted] **20[redacted] URINE LEUK ESTERASE:** Results: Large; Normal range: Negative

[redacted] 20[redacted] URINE WHITE BLOOD CELLS: 6-10 hpf

[redacted] **20[redacted] VENOUS LACTIC ACID:** 0.9 MMOL/L (normal 0.5 to 2.2)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 12.20 k/uL (normal 3.7 to 10.3)

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			
肝脾腫大				X
急性膵炎	X			

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

Medical History	Onset Year
LATENT TUBERCULOSIS	Not reported.
CROHN'S DISEASE	20[redacted]
CARDIAC ARRHYTHMIA: PAROXYSMAL TACHYCARDIA	20[redacted]
SLEEP APNEA: OBSTRUCTIVE SLEEP APNEA	20[redacted]
DRUG ALLERGIES/REACTIONS: DRUG INDUCED LUPUS FROM REACTION TO INFLIXIMAB	20[redacted]
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
OTHER: VITAMIN D DEFICIENCY	20[redacted]
TUBERCULOSIS: LATENT TB- TREATED WITH RIFAMPIN X4 MONTHS CHESR XRAY [redacted] 20[redacted] NO EVIDENCE OF ACTIVE TB	20[redacted]
IMMUNE DEFICIENCY DISEASE: LUPUS INDUCED BY REACTION TO INFLIXIMAB- RESOLVED [redacted]-20[redacted]	20[redacted]
OTHER: INFLAMMATORY POLYARTHROPATHY	20[redacted]
OTHER: PERICARDITIS	20[redacted]
OTHER: INCOMPLETE RIGHT BUNDLE BRANCH BLOCK ON EKG	20[redacted]

Prior Procedures	Procedure Year
SURGERY: WISDOM TEETH REMOVED	20[redacted]
SURGERY: KNEE SURGERY X2 FOR MENISCAL TEAR	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): BIOPSY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CIGARETTES	FORMER	15 CIGARETTE	5	20[redacted]
CHEWING TOBACCO	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
RIFAMPICIN	600 MG mg	QD	Y-M: 20[redacted]
INFLIXIMAB	500 mg	Not reported.	Y-M: 20[redacted] / -312
BISACODYL	10 MG mg	OTHER: AT 9PM	Y-M: 20[redacted] / -15
FENTANYL	100 MCG (25MCG/0.5ML) OTHER: MCG	PRN	Y-M: 20[redacted] / -14
LIDOCAINE	20 MG mg	PRN	Y-M: 20[redacted] / -14
MIDAZOLAM	25 MG mg	PRN	Y-M: 20[redacted] / -14
PROPOFOL	300 MG mg	OTHER: GIVEN DURING PROCEDURE	Y-M: 20[redacted] / -14
SODIUM CHLORIDE	500 ML mL	OTHER: DURING PROCEDURE	Y-M: 20[redacted] / -14

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 92
HYDROMORPHONE	1 mg	PRN	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
MORPHINE	4 mg	PRN	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
BACTERIAL AND VIRAL VACCINES, COMBINED	1 mL	OTHER: 1 DOSE	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 43
METHYLPREDNISOLONE	60 mg	OTHER: 1 DOSE	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 43
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 44
HYDROMORPHONE	0.5 mg	PRN	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 44
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 44

RINGER-LACTATE	1000 ML AT 125CC/HR X24 HOURS OTHER: 125 CC/HR	OTHER: 24 HOURS	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 44
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 49
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 44	ONGOING
NALOXONE	4 mg	PRN	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 49
OXYCODONE	15 mg	PRN	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 49
VEDOLIZUMAB	300 mg	OTHER: EVERY 2 WEEKS	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 77
PIP/TAZO	3.375 g	OTHER: X1	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 79
VANCOMYCIN	1.5 g	OTHER: ONCE	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 79
MORPHINE	4 mg	PRN	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 80
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 81
SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 81
METHYLPREDNISOLONE	60 mg	OTHER: ONCE	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 80
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 81
HYDROMORPHONE	2 mg	PRN	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 81
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 81
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 81	ONGOING
OXYCODONE	15 mg	PRN	Y-M: 20[redacted] / 81	ONGOING
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 81
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 87	ONGOING
MORPHINE	2 mg	PRN	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 87
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 92
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 92

COLCHICINE	0.6 mg	BID	Y-M: 20[redacted] / 91	ONGOING
IBUPROFEN	600 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 92	ONGOING
USTEKINUMAB	390 mg	OTHER: EVERY MONTH	Y-M: 20[redacted] / 94	ONGOING
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / 102	ONGOING
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 113	ONGOING
HYDROMORPHONE	1 OTHER: MG/ML	PRN	Y-M: 20[redacted] / 113	ONGOING
PROMETHAZINE	25 mg	PRN	Y-M: 20[redacted] / 113	ONGOING
RINGER-LACTATE	200 mL	OTHER: PER HOUR	Y-M: 20[redacted] / 113	ONGOING
AMIDOTRIZOIC ACID	30 OTHER: CC	OTHER: ONCE	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
KETOROLAC	30 mg	OTHER: ONCE	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
PROCHLORPERAZINE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
SODIUM CHLORIDE	999 OTHER: CC/HR	OTHER: ONE TIME	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF CD
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 37 (8 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 42): Activated Partial Thromboplastin Time: 30 [23.4 - 36.1] sec; Alanine Aminotransferase: 21 [16 - 61] IU/L; Albumin: 3.5 [3.4 - 5] g/dL; Alkaline Phosphatase: 127 [45 - 117] IU/L; Aspartate Aminotransferase: 11 [15 - 37] IU/L; Hematocrit: 41.7 [42 - 52] %; Hemoglobin: 13.8 [14 - 18] g/dL; Leukocytes: 10.7 [4.8 - 10.8] 10^3/uL; Lipase: 164 [73 - 393] U/L; NPTST054-C-REACTIVE PROTEIN: .73 [0 - 0.3] mg/dL; NPTST149-LACTATE: 0.7 [0.4 - 2] mmol/L; NPTST205-PROTEIN, TOTAL: 8.1 [6.4 - 8.2] g/dL; Platelets: 399 [130 - 400] 10^3/uL; Prothrombin Time: 14.5 [11.7 - 14.4] sec

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 40): CT ABDOMEN PELVIS WITHOUT CONTRAST: 1.MILD PERICOLONIC FAT STRANDING IN PROXIMAL SIGMOID COLON WHICH MAY REFLECT A NONSPECIFIC COLITIS.MAY REFLECT MILD INFLAMMATION FROM UNDERLYING KNOWN INFLAMMATORY BOWEL DISEASE. 2.COLONIC DIVIRTICULOSIS 3.SMALL HIATAL HERNIA 4HEPATOSPLENAMEGALY 5.ADDITIONAL INCIDENTAL FINDINGS AS ABOVE. NOTE THAT

ASSESSMENT OF THE VISCERAL STRUCTURES OF THE ABDOMEN AND PELVIS PARTLY LIMITED BY LACK OF IV CONTRAST

AE Stopped Rx Day	44 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	EXACERBATION OF CROHN'S DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Event of Interest - Hepatic Events

Event Description	HEPATOSPLENOMEGALY
Preferred term	肝脾腫大
AE Onset Date / Rx Day	[redacted]20[redacted] / 42 (13 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

Not Applicable

Microbiology

Not Applicable

SAE Supplemental Procedure

Not Applicable

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	Not Applicable
Discontinued Study Drug Due to the Event	NO
SAE Criteria	None

Event #3: Serious Adverse Event

Event Description	CROHN'S DISEASE FLARE
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 78 (49 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 79): Albumin: 3.3 [3.4 - 5] g/dL; Alkaline Phosphatase: 160 [45 - 117] IU/L; C Reactive Protein: 3.81 [0 - 0.3] mg/L; Leukocytes: 11.2 [4.8 - 10.8] 10^3/uL; NPTST149-LACTATE: 0.8 [0.4 - 2] mmol/L; NPTST286-WESTERGREN ESR: 54 [0 - 15] mm/h; [redacted]20[redacted] (Rx Day 80): NPTST078-D-DIMER: 2.16 [0 - 0.49] ug/mL; NPTST103-FIBRINOGEN: 455 [180 - 467] mg/dL; [redacted]20[redacted] (Rx Day 81): Leukocytes: 9.3 [4.8 - 10.8] 10^3/uL

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 71): ADULT ECHOCARDIPGRAM: LEFT VENTRICLE IS OF NORMAL DIMENSIONS. NORMAL LV SYSTOLIC FUNCTION. LVEF ESTIMATED 50-55% RIGHT VENTRICLE IS OF NORMAL DIMENSIONS.RIGHT VENTRICULAR SYSTOLIC FUNCTION IS NORMAL. NORMAL ATRIAL SIZES.TRIVIAL-TO-SMALL PERICARDIAL EFFUSION.THE EFFUSION HAS NOT INCREASED IN SIZE WHEN COMPARED W/PRIOR ECHOCARDIOGRAM FROM [redacted]/20[redacted] UNABLE TO ESTIMATE THE PULMONARY ARTERY SYSTOLIC PRESSURE; CHEST XRAY 1 VIEW: INTERVAL DEVELOPMENT OF A PATCHY AIRSPACE OPACITY IN THE LEFT LOWER LOBE. FINDINGS FAVOR PNEUMONIA, BUT ATELECTASIS IS ALSO A CONSIDERATION GIVEN THE LOW LUNG VOLUMES.; CT ABDOMEN/PELVIS W/OUT CONTRAST: SMALL-MODERATE PERICARDIAL FLUID W/SUSPECTED MILD DIFFUSE PERICARDIAL THICKENING, SUBOPTIMALLY ASSESSED.FINDINGS CONCERNING FOR NONSPECIFIC PERICARDITIS.RECOMMEND CLINICAL CORRELATION & FURTHER EVALUATION W/ECHOCARDIOGRAPHY.A FEW LOOPS OF BORDERLINE PROMINENT PROXIMAL SMALL BOWEL MEASURE <3 CM DIAMETER W/O FOCAL DISCRETE TRANSITION POINT IDENTIFIED, SUGGESTING MILD NONSPECIFIC/REACTIVE ILEUS.AREASOF EQUIVOCAL ILEAL WALL THICKENING VS APPEARANCE ACCENTUATED BY DECOMPRESSION.SUBTLE STRANDING IN FAT ADJACENT TO PROXIMAL SIGMOID COLON.?SUBTLE MILD NONSPEC SEGMENTAL COLITIS VS EARLY ACUTE DIVERTIC

AE Stopped Rx Day	81 (52 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CROHN'S DISEASE EXACERBATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #4: Serious Adverse Event

Event Description	CROHN'S DISEASE EXACERBATION
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 87 (58 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 87): Leukocytes: 11.5 [4.8 - 10.8] 10^3/uL; [redacted]20[redacted] (Rx Day 88): C Reactive Protein: 0.14 [0 - 0.3] mg/dL; NPTST149-LACTATE: 3.1 [0.4 - 2] mmol/L; [redacted]20[redacted] (Rx Day 91): Erythrocytes: 4.5 [4.7 - 6.1] 10^6/uL; Leukocytes: 15.1 [4.8 - 10.8] 10^3/uL; [redacted]20[redacted] (Rx Day 92): Leukocytes: 13.9 [4.8 - 10.8] 10^3/uL

Microbiology

[redacted]20[redacted] (Rx Day 88): BLOOD NPTST044-BLOOD CULTURES: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 71): MRI OF PELVIS/ABDOMEN: IMPRESSION: KNOWN CROHN'S DISEASE. FINDINGS SUGGESTIVE OF ACUTE/ACTIVE INFLAMMATION INVOLVING CECUM, TERMINAL ILEUM, DISTAL ILEAL LOOPS WITHIN THE RIGHT LOWER QUADRANT AND A S HORT SEGMENT OF THE SIGMOID COLON; RAD EXAM, ABD, COMPLETE, ACUTE ABD SERIES (ABD VIEWS W/CHEST): 1. MODERATE STOOL BURDEN IN THE CECUM AND ASCENDING COLON WITHOUT EVIDENCE OF TOXIC MEGACOLON. 2.LIKELY MILD ILEUS. 3.NO ACUTE CARDIOPULMONARY FINDINGS.

AE Stopped Rx Day	92 (63 DAYS AFTER LAST TREATMENT)
Duration of AE	6 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NATURAL PROGRESSION OF THE DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #5: Serious Adverse Event

Event Description	ACUTE PANCREATITIS, UNSPECIFIED
Preferred term	急性膵炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 113 (84 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 79): Platelets: 493 [130 - 400] 10^3/uL; [redacted]20[redacted] (Rx Day 113): Albumin: 3.7 [3.4 - 5] g/dL; Aspartate Aminotransferase: 14 [15 - 37] IU/L; Blood Urea Nitrogen: 18 [7 - 18] mg/dL; Hematocrit: 41.6 [42 - 52] %; Hemoglobin: 14.3 [14 - 18] g/dL; Leukocytes: 9.8 [4.8 - 10.8] 10^3/uL; Lipase: 1407 [73 - 393] U/L; Platelets: 337 [130 - 400] 10^3/uL; [redacted]20[redacted] (Rx Day 115): Calcium: 8.6 [8.5 - 10.1] mg/dL; NPTST049-C DIFF TOX B GENE PCR: NEGATIVE [Not reported - Not reported] Unit not reported; [redacted]20[redacted] (Rx Day 116): Albumin: 3.2 [3.4 - 5] g/dL; Hematocrit: 39.1 [42 - 52] %; Hemoglobin: 13.0 [14 - 18] g/dL; [redacted]20[redacted] (Rx Day 130): Lipase: 144 [73 - 393] U/L

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 102): COLONOSCOPY: COLONOSCOPY [redacted]/20[redacted] WITHOUT FOCAL ABNORMALITIES, NO STRICTURES OR FISTULAS WERE NOTED. BIOPSY WAS WITHOUT SIGNIFICANT INFLAMMATION.; CT ABDOMEN/PELVIS WITHOUT CONTRAS: 1. LIMITED EXAMINATION WITHOUT INTRAVENOUS CONTRAST. 2. THE TERMINAL ILEUM, CECUM, AND APPENDIX ARE UNREMARKABLE. 3. SCATTERED PROMINENT MESENTERIC AND RETROPERITONEAL LYMPH NODES, LIKELY REACTIVE GIVEN THE ONGOING INFLAMMATORY PROCESSES. 4. NO EVIDENCE OF BOWEL OBSTRUCTION. 5. NO LOCULATED FLUID COLLECTIONS TO SUGGEST ABSCESS. NO FREE INTRAPERITONEAL A IR OR FLUID.; ULTRASOUND ABDOMINAL, LIMITED: IMPRESSION: 1. HEPATOSPLENOMEGALY. NO FOCAL HEPATIC MASSES. 2. NO EVIDENCE OF GALLSTONES OR ACUTE CHOLECYSTITIS. 3. THE PANCREAS IS NOT WELL SEEN DUE TO OVERLYI NG BOWEL GAS.

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PRESUMED ACUTE PANCREATITIS, PRESENTING W/ABDOMINAL PAIN, NAUSEA AND VOMITING, ALONG W/ ELEVATED LIPASE, MEETING DIAGNOSTIC CRITERIA FOR ACUTE PANCREATITIS/MOST LIKELY DRUG INDUCED
Discontinued Study Drug Due to the Event	NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

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，クローン病の増悪の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元喫煙者（1 日 15 本を 5 年間），クローン病，インフリキシマブに対する薬剤誘発性ループス，鉄欠乏性貧血，炎症性多発性関節障害，心膜炎及び心電図上の不完全右脚ブロックであった。

投与 37 日後，被験者はクローン病増悪を発現した。投与 44 日後，クローン病の増悪は消失した。

被験者はクローン病（既往）のフレアである 5 日間にわたる腹痛悪化のため，救急治療室を受診した。被験者は，非血性下痢便が 1 日 5 回あるが，嘔吐はないと報告した。投与 43 日後，被験者は入院した。CT スキャンが行われ，S 状結腸に軽度の大腸炎が認められた。下痢は病院で軽快し，有形便となった。被験者の食事は通常食となった。治験薬の投与は中止された。投与 44 日後，被験者は退院した。

投与された薬剤は，乳酸リンゲル液，オンダンセトロン，methylprednisone，オキシコドン，モルヒネ，Dilaudid 及びエノキサパリンであった。

Causality for RISANKIZUMAB (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of EXACERBATION OF CROHN'S DISEASE

- Investigator: Exacerbation of Crohn's Disease.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 3.5 G/DL (normal 3.4 to 5.0)

[redacted] **20[redacted] CT ABDOMEN PELVIS WITHOUT CONTRAST:** 1. MILD PERICOLONIC FAT STRANDING IN PROXIMAL SIGMOID COLON WHICH MAY REFLECT A NONSPECIFIC COLITIS.MAY REFLECT MILD INFLAMMATION FROM UNDERLYING KNOWN INFLAMMATORY BOWEL DISEASE. 2. COLONIC DIVIRTICULOSIS 3. SMALL HIATAL HERNIA 4. HEPATOSPLENAMEGALY 5. ADDITIONAL INCIDENTAL FINDINGS AS ABOVE. NOTE THAT ASSESSMENT OF THE VISCERAL STRUCTURES OF THE ABDOMEN AND PELVIS PARTLY LIMITED BY LACK OF IV CONTRAST

[redacted] **20[redacted] HCT:** 41.7 % (normal 42 to 52)

[redacted] **20[redacted] HGB:** 13.8 G/DL (normal 14 to 18)

[redacted] **20[redacted] PLATELET COUNT:** 399 X10**3/MCL (normal 130 to 400)

[redacted] **20[redacted] PROTEIN:** 8.1 G/DL (normal 6.4 to 8.2)

[redacted] **20[redacted] WBC:** 10.7 X10**3/MCL (normal 4.8 to 10.8)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

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 ABBV-066（リサンキズマブ）の治験で盲検化された治験薬が投与され，クローン病フレアの事象を発現した。

Event 3 の臨床経過：

関連する病歴は，元喫煙者（1 日 15 本を 5 年間），クローン病，インフリキシマブに対する薬剤誘発性ループス，鉄欠乏性貧血，ビタミン D 欠乏，免疫不全症，結腸憩室症，肝脾腫大，小裂孔ヘルニア及び元軽度飲酒者であった。

本事象発現前の投与 37 日後，被験者はクローン病増悪を発現し，[redacted] に報告された。

投与 78 日後，被験者はクローン病フレアを発現した。投与 81 日後，クローン病フレアは消失した。

本事象発現前の投与 77 日後，被験者はベドリズマブ点滴静注の最終投与を受けた。被験者は，投与 78 日後に始まった腹痛及び直腸出血を主訴として救急治療室を受診した。被験者によれば，腹痛は鋭く，広範囲にわたっており，重度で，非放散性であった。腹痛は，悪心及び／又は食事の嘔吐（非出血性）を伴っていた。また，便中にタール色の血液が認められた（2 回）。投与 78 日後，被験者は息切れ及び胸骨下に非放散性の胸膜性胸痛があり，夜中に目が覚めた。胸痛及び息切れは仰臥位で悪化し，座位で改善した。被験者によれば，この胸痛は過去に心膜炎で入院した時にあった痛みと類似していた。投与 79 日後，被験者は入院した。被験者は IV 補液，疼痛治療剤，IV ステロイド剤に対して反応を示した。投与 81 日後，被験者は退院し，外来での経過観察となった。

投与された薬剤は，塩化ナトリウム，オンダンセトロン，オキシコドン，モルヒネ，ヒドロモルフォン，トラマドール，アセトアミノフェン，ソル・メドロール，バンコマイシン及びゾシンであった。

The patient’s past medications include:

RIFAMPIN for LATENT TUBERCULOSIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for ABBV-066 (Blinded)

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1) Crohn's disease aggravated (10011403) (Crohn's disease (10011401)) [v.21.1] [10011403]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABBV-066 (Blinded)

Event of CROHN'S DISEASE FLARE

- Investigator: CROHN'S DISEASE EXACERBATION

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ACTIVATED PARTIAL THROMBOPLASTIN TIME: 37 SEC (normal 23.4 to 36.1)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 31 IU/L (normal 16 to 61)

[redacted] **20[redacted] ALBUMIN:** 3.3 G/DL (normal 3.4 to 5.0)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 160 IU/L (normal 45 to 117)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 9 IU/L (normal 15 to 37)

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 3.81 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CHEST X-RAY:** INTERVAL DEVELOPMENT OF A PATCHY AIRSPACE OPACITY IN THE LEFT LOWER LOBE. FINDINGS FAVOR PNEUMONIA, BUT ATELECTASIS IS ALSO A CONSIDERATION GIVEN THE LOW LUNG VOLUMES.

[redacted] **20[redacted] D-DIMER:** 2.16 MCG/ML (normal 0 to 0.49)

[redacted] **20[redacted] ECHOCARDIOGRAM:** LEFT VENTRICLE IS OF NORMAL DIMENSIONS. NORMAL LV SYSTOLIC FUNCTION. LVEF ESTIMATED 50-55% RIGHT VENTRICLE IS OF NORMAL DIMENSIONS.RIGHT VENTRICULAR SYSTOLIC FUNCTION IS NORMAL. NORMAL ATRIAL SIZES. TRIVIAL-TO-SMALL PERICARDIAL EFFUSION.THE EFFUSION HAS NOT INCREASED IN SIZE WHEN COMPARED W/PRIOR ECHOCARDIOGRAM FROM [redacted]/20[redacted] UNABLE TO ESTIMATE THE PULMONARYARTERY SYSTOLIC PRESSURE

[redacted] **20[redacted] ESR:** 54 MM/HR (normal 0 to 15)

[redacted] **20[redacted] FIBRINOGEN:** 455 mg/dL (normal 180 to 467)

[redacted] **20[redacted] HEMATOCRIT:** 40.9 % (normal 42 to 52)

[redacted] **20[redacted] HEMATOCRIT:** 36.5 % (normal 42 to 52)

[redacted] 20[redacted] **HEMOGLOBIN:** 13.9 G/DL (normal 14 to 18)

[redacted] 20[redacted] **HEMOGLOBIN:** 12.1 G/DL (normal 14 to 18)

[redacted] 20[redacted] **LIPASE:** 95 U/L (normal 73 to 393)

[redacted] 20[redacted] **PLATELET COUNT:** 493 X10**3/MCL (normal 130 to 400)

[redacted] 20[redacted] **PLATELET COUNT:** 442 10e3/uL (normal 130 to 400)

[redacted] 20[redacted] **PROTEIN:** 7.8 G/DL (normal 6.4 to 8.2)

[redacted] 20[redacted] **PROTHROMBIN TIME:** 14.2 SEC (normal 11.7 to 14.4)

[redacted] 20[redacted] **TROPONIN:** 0 NG/ML (normal 0 to 0.10)

[redacted] 20[redacted] **URINE:** 0.8 MMOL/L (normal 0.4 to 2.0)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 11.2 X10**3/MCL (normal 4.8 to 10.8)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 9.3 X10**3/MCL (normal 4.8 to 10.8)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

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，クローン病増悪の事象を発現した。

Event 4 の臨床経過：

関連する病歴は，クローン病，鉄欠乏性貧血，結腸憩室症，肝脾腫大，小裂孔ヘルニア，元喫煙者（1 日 15 本を 5 年間）及び元飲酒者（1 日 2 杯未満）であった。

投与 87 日後，被験者はクローン病増悪を発現した。投与 92 日後，クローン病増悪は消失した。

本事象発現前の投与 37 日後，被験者はクローン病増悪のため入院し，その際に治験薬の投与が中止された（AER # [redacted]）。投与 79 日後，被験者はクローン病フレアのため入院した（AER [redacted]）。被験者は prednisone を処方され，帰宅した。退院以降，被験者は右側の腹痛，悪心，未消化食物の嘔吐（非出血性）及びゆるい便の持続を報告した。

投与 87 日後，被験者は刺すような非放散性の持続する疼痛のため，救急治療室を受診した。被験者は自己判断でゾフラン及びオキシコドンを服用しており，疼痛はわずかに軽快した。被

験者はIV疼痛治療剤を要求していた。被験者はIV補液，制吐剤，ステロイド剤及び疼痛治療剤による治療が行われ，疼痛は軽快した。入院中，被験者は左側の非放散性胸痛も訴え，被験者によれば，これらの症状は過去に心膜炎と診断されたときに経験した症状と類似していた。被験者は，心膜炎の疑いのため心臓医の診察を受けた。被験者は，これらの症状が投与の約4か月前に罹患した病歴の心膜炎と類似していることを伝えた。被験者は薬剤及びテレメトリーによる治療を受けた。投与92日後，被験者は退院した。

本事象により治験薬の投与が完全に中止された。

投与された薬剤は，パントプラゾール，アセトアミノフェン，メチルプレドニゾロン及びモルヒネであった。

The patient’s past medications include:

MESALAMINE for CROHN'S DISEASE ([redacted])

INFLIXIMAB for CROHN'S DISEASE ([redacted])

MORPHINE for ABDOMINAL PAIN ([redacted])

ACETAMINOPHEN for ABDOMINAL PAIN ([redacted])

HYDROMORPHONE for ABDOMINAL PAIN ([redacted])

TRAMADOL for ABDOMINAL PAIN ([redacted])

Causality for RISANKIZUMAB (Blinded)

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

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of CROHN'S DISEASE EXACERBATION

- Investigator: NATURAL PROGRESSION OF THE DISEASE

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD CULTURE: Negative

[redacted] **20[redacted] COMPLETE ABDOMINAL SERIES (ABDOMINAL VIEWS WITH CHEST):** 1. Moderate stool burden in the cecum and ascending colon without evidence of toxic megacolon. 2. Likely mild ileus. 3. No acute cardiopulmonary findings

[redacted] **20[redacted] HIGH SENSIVITIY CRP:** 0.14 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] LACTATE:** 3.1 MMOL/L (normal 0.4 to 2.0)

[redacted] **20[redacted] MRI OF ABDOMEN/PELVIS:** Impression: known Crohn's disease. Findings suggestive of acute/active inflammation involving cecum, terminal ileum, distal ileal loops within the right lower quadrant and a short segment of the sigmoid colon

[redacted] **20[redacted] RBC:** 4.5 X10**6/MCL (normal 4.7 to 6.1)

[redacted] **20[redacted] WBC:** 11.5 X10**3/MCL (normal 4.8 to 10.8)

[redacted] **20[redacted] WBC:** 15.1 X10**3/MCL (normal 4.8 to 10.8)

[redacted] **20[redacted] WBC:** 13.9 X10**3/MCL (normal 4.8 to 10.8)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

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，急性膵炎（詳細不明）の事象を発現した。

Event 5 の臨床経過：

関連する病歴は，元喫煙者（1 日 15 本），クローン病（L3：回腸・結腸，非狭窄・非穿通型），閉塞性睡眠時無呼吸，発作性頻脈，インフリキシマブに対する薬剤誘発性ループス，鉄欠乏性貧血，潜在性結核（TB：Rifampin による治療が 4 ヵ月間行われた），炎症性多発性関節障害，心膜炎，心電図上の不完全右脚ブロック，結腸憩室症，肝脾腫大及び元軽度飲酒者（1 日 2 杯未満）であった。

投与 113 日後，被験者は急性膵炎（詳細不明）を発現した。

投与 113 日後，被験者は悪心及び嘔吐を伴う（主に上腹部の）背部に放散する腹痛のため入院した。被験者によれば，この疼痛は当月初旬に結腸内視鏡検査を受ける前に始まった。被験者は発熱を否定したが，悪寒は報告した。被験者は排便習慣の変化を否定し，入院時の排便習慣は軟便～水様便を 1 日 3～4 回であった。被験者は吐血，メレナ又は血便排泄も否定し，最近のアルコール摂取又は最近の旅行も否定した。投与 79 日後，被験者はクローン病フレアのため入院しており（AER#: [redacted] に詳述），その際にエンタイビオの導入用量の投与を受けている。その後の投与から約 3 か月後，ステラーラと prednisone によるブリッジング療法が開始された。現在の入院の 1 週間前まで，この療法による被験者の状態は良好であった。臨床検査，腹部超音波検査及び腹部 CT スキャンが行われた。CT スキャンの所見は，投与から約 3 か月後に行われた MRI の所見と類似していた。急性膵炎は薬剤誘発性膵炎の可能性が高い（ただし，自己免疫性膵炎又は特発性膵炎の可能性もあり）と診断された。疼痛は Dilaudid の経口投与によりコントロール良好であった。経口で液体及び低脂肪食の摂取が可能であった。膵炎の原因である可能性を考慮し，コルヒチン，イブプロフェン，ブデソニドの投与が中止された。投与 117 日後，被験者はトラマドール及びタイレノールを処方され，退院した。

投与された薬剤は，トラマドール，タイレノール，プロメタジン，生理食塩水，ケトロラク，Compazine，エノキサパリン，ヒドロモルフォン及び乳酸リンゲル液であった。

The patient’s past medications include:

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

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

Causality for RISANKIZUMAB (Blinded)

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1) Acute pancreatitis (10000971) (Pancreatitis acute (10033647)) [v.22.0] [10000971]

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 ACUTE PANCREATITIS, UNSPECIFIED

- Investigator: Presumed acute pancreatitis, presenting with abdominal pain, nausea and vomiting, along with elevated lipase, meeting diagnostic criteria for acute pancreatitis/most likely drug induced.

- AbbVie: Risk factor includes pre-existing Crohns disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Impression: 1. Hepatosplenomegaly. No focal hepatic masses. 2. No evidence of gallstones or acute cholecystitis. 3. The pancreas is not well seen due to overlying bowel gas.

[redacted] **20[redacted] ALBUMIN:** 3.7 G/DL (normal 3.4 to 5.0)

[redacted] **20[redacted] ALBUMIN:** 3.2 G/DL (normal 3.4 to 5.0)

[redacted] 20[redacted] ASPARTATE AMINOTRANSFERASE: 14 IU/L (normal 15 to 37)

[redacted] **20[redacted] BUN:** 18 mg/dL (normal 7 to 18)

[redacted] **20[redacted] CALCIUM:** 8.0 mg/dL (normal 8.5 to 10.1)

[redacted] **20[redacted] COLONOSCOPY:** COLONOSCOPY [redacted]/[redacted]/20[redacted] WITHOUT FOCAL ABNORMALITIES, NO STRICTURES OR FISTULAS WERE NOTED. BIOPSY WAS WITHOUT SIGNIFICANT INFLAMMATION.

[redacted] **20[redacted] CT OF ABDOMEN:** Abdomen/pelvis: 1. Limited examination without intravenous contrast. 2. The terminal ileum, cecum, and appendix are unremarkable. 3. Scattered prominent mesenteric and retroperitoneal lymph nodes, likely reactive given the ongoing inflammatory processes. 4. No evidence of bowel obstruction. 5. No loculated fluid collections to suggest abscess. No free intraperitoneal air or fluid.

[redacted] **20[redacted] HEMATOCRIT:** 41.6 % (normal 42 to 52)

[redacted] **20[redacted] HEMATOCRIT:** 39.1 % (normal 42 to 52)

[redacted] **20[redacted] HEMOGLOBIN:** 14.3 G/DL (normal 14 to 18)

[redacted] **20[redacted] HEMOGLOBIN:** 13.0 G/DL (normal 14 to 18)

Unknown date IGG: Igg4 pending for autoimmune pancreatitis

[redacted] **20[redacted] LIPASE:** 1407 U/L (normal 73 to 393)

[redacted] **20[redacted] LIPASE:** 144 U/L (normal 73 to 393)

[redacted] **20[redacted] PCR:** Specimen: stool; C. Difficile tox B gene PCR: negative

[redacted] **20[redacted] PLATELET COUNT:** 337 10^3/uL (normal 130 to 400)

[redacted] **20[redacted] WBC:** 9.8 10^3/uL (normal 4.8 to 108)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ASTHMA: CHILDHOOD ASTHMA	19[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: ENDOMETRIOSIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: CROHNS COLITIS	20[redacted]
OTHER: VULVOVAGINOPLASTY	20[redacted]
OTHER: CERVICAL DYSPLASIA	20[redacted]
OTHER: CESAREAN SECTION	20[redacted]
OTHER: GENERALIZED ABDOMINAL PAIN. EGD/ COLONOSCOPY	20[redacted]
OTHER: CLOSED FRACTURE DISTAL END OF RIGHT WRIST	20[redacted]
OTHER: OVARIAN CYSTS	20[redacted]
OTHER: PERIPHERAL ARTHROPATHY	20[redacted]
OTHER: GASTROENTERITIS	20[redacted]
OTHER: IRRITABLE BOWEL DISEASE	20[redacted]
OTHER: ACNE FACE	20[redacted]
ANEMIA: CROHNS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: PANCOLITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: WISDOM TEETH EXTRACTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: DIAGNOSTIC LAPARSCOPY	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): BIOPSY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CIGARETTES	FORMER	10 CIGARETTE	3	20[redacted]
CHEWING TOBACCO	UNKNOWN	Not reported.	.	Not reported.
CIGARS	UNKNOWN	Not reported.	.	Not reported.
E-CIGARETTES	UNKNOWN	Not reported.	.	Not reported.

PIPES	UNKNOWN	Not reported.	.	Not reported.

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
NORLESTRIN FE	1 OTHER: TABLET	QD	Y-M: 20[redacted]
SPIRONOLACTONE	100 mg	QD	Y-M: 20[redacted] / -289
MENTHA X PIPERITA	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / -136
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -136
MESALAZINE	1.2 g	BID	Y-M: 20[redacted] / -135
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -74
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -59
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -52
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -45
BISACODYL	20 mg	OTHER: ONCE	Y-M: 20[redacted] / -8
MACROGOL 3350	238 g	OTHER: ONCE	Y-M: 20[redacted] / -8
FLEBOBAG RING LACT	500 mL	OTHER: ONCE	Y-M: 20[redacted] / -7
LIDOCAINE	60 mg	OTHER: ONCE	Y-M: 20[redacted] / -7
PROPOFOL	300 mg	OTHER: ONCE	Y-M: 20[redacted] / -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
NORLESTRIN FE	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
SPIRONOLACTONE	100 mg	QD	Y-M: 20[redacted] / -289	ONGOING
MENTHA X PIPERITA	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / -136	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -136	ONGOING
BISACODYL	20 mg	OTHER: ONCE	Y-M: 20[redacted] / -8	Y-M: 20[redacted] / -8
MACROGOL 3350	238 g	OTHER: ONCE	Y-M: 20[redacted] / -8	Y-M: 20[redacted] / -8
FLEBOBAG RING LACT	500 mL	OTHER: ONCE	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -7

LIDOCAINE	60 mg	OTHER: ONCE	Y-M: 20[redacted] / - 7	Y-M: 20[redacted] / - 7
PROPOFOL	300 mg	OTHER: ONCE	Y-M: 20[redacted] / - 7	Y-M: 20[redacted] / - 7
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / 17	ONGOING
MORPHINE	4 mg	PRN	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 21
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 21
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 21
SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 21
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 26
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 30
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 30

Event #1: Serious Adverse Event

Event Description	WORSENING CROHNS, PANCOLITIS
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 17
Age at AE Onset	2[redacted]
Laboratory Testing	
[redacted]20[redacted] (Rx Day 20): Monocytes/Leukocytes: 1.3 [0 - 0.8] %	
Microbiology	
[redacted]20[redacted] (Rx Day 20): URINE NPTST266-UA: NEGATIVE	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx Day 15): CT SCAN: PANCOLITIS	
AE Stopped Rx Day	21
Duration of AE	5 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	WORSENING CROHNS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	WORSENING CROHNS, PANCOLITIS
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 17
Age at AE Onset	2[redacted]
Laboratory Testing	
[redacted]20[redacted] (Rx Day 20): Monocytes/Leukocytes: 1.3 [0 - 0.8] %	
Microbiology	
[redacted]20[redacted] (Rx Day 20): URINE NPTST266-UA: NEGATIVE	
SAE Supplemental Procedure	
[redacted]20[redacted] (Rx Day 15): CT SCAN: PANCOLITIS	
AE Stopped Rx Day	21
Duration of AE	5 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	WORSENING CROHNS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

米国の治験責任医師からの報告。本被験者は 2[redacted] 歳女性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，クローン病悪化（汎大腸炎）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，クローン病，クローン大腸炎，全身性腹痛，EGD／結腸内視鏡検査，元紙巻きタバコ喫煙者（1 日 0.5 箱を 3 年間），卵巣嚢胞，胃腸炎，過敏性大腸疾患，胃食道逆流性疾患，汎大腸炎及び現軽度飲酒者（1 日 2 杯未満）であった。

投与 17 日後，被験者はクローン病悪化（汎大腸炎）を発現した。投与 21 日後，クローン病悪化（汎大腸炎）は消失した。

本事象発現の 1 週間前，被験者は腹痛を訴え，当初あった下痢は Imodium により改善した。

投与 20 日後，被験者は入院した。被験者はベースライン来院を完了した。投与の約 1 か月後，被験者は CT 検査を受け，汎大腸炎が認められた。被験者は，下腹部痛が 7/10 であると訴えた。出血，下痢及び微熱は認められなかった。バイタルサインは安定していた。疼痛はステロイド剤及び抗生剤により改善した。

投与 21 日後，被験者は退院した。

治験責任医師は，子どもの病気及び新しい仕事のストレスを本事象のリスク因子であると判断した。

投与された薬剤は，塩化ナトリウム，オンダンセトロン，モルヒネ，シプロフロキサシン，メトロニダゾール，Imodium，シプロフロキサシン及び prednisone であった。

The patient’s past medications include:

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

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

Causality for RISANKIZUMAB (Blinded)

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1) Pancolitis (10033573) (Colitis (10009887)) [v.22.0] [10033573]

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

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

Dechallenge: Not Applicable

2) Crohns disease aggravated (10011408) (Crohn's disease (10011401)) [v.22.0] [10011408]

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of WORSENING CROHNS, PANCOLITIS

- Investigator: PANCOLITIS RELATED TO QUESTIONABLE PLACEBO

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CT SCAN: pancolitis

[redacted] **20[redacted] MONOCYTES %:** 1.3 % (normal 0.0 to 0.8)

[redacted] 20[redacted] URINE TEST: 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
腹部膿瘍		X		
小腸閉塞	X	X		

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	2[redacted]	MALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
PEPTIC ULCER DISEASE: PEPTIC ULCER	20[redacted]
OTHER: PERIRECTAL ABCESS	20[redacted]
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: ENTEROCOLIC FISTULA	20[redacted]
OTHER: STOMACH ULCER	20[redacted]

Prior Procedures	Procedure Year
CROHN'S DISEASE SURGICAL HISTORY: SETONS REMOVED	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: CLOSURE OF ENTEROCOLIC FISTULA	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: PLACEMENTS OF SETONS	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): BIOPSY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CIGARETTES	FORMER	2 CIGARETTE	2	20[redacted]
E-CIGARETTES	FORMER	2 SESSIONS	0.25	20[redacted]
CHEWING TOBACCO	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
BUDESONIDE	3 mg	TID	Y-M: 20[redacted]
INFLIXIMAB	UNK IU/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
MESALAZINE	1.2 g	BID	Y-M: 20[redacted]
PREDNISONE	5 mg	OTHER: 8 TABLETS DAILY TAPER	Y-M: 20[redacted] / -146
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -124
LIDOCAINE	60 mg	OTHER: ONCE FOR COLONOSCOPY	Y-M: 20[redacted] / -18
PROPOFOL	100 mg	OTHER: ONCE FOR COLOSCOPY	Y-M: 20[redacted] / -18

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -124	ONGOING
LIDOCAINE	60 mg	OTHER: ONCE FOR COLONOSCOPY	Y-M: 20[redacted] / -18	Y-M: 20[redacted] / -18
PROPOFOL	100 mg	OTHER: ONCE FOR COLOSCOPY	Y-M: 20[redacted] / -18	Y-M: 20[redacted] / -18
FUROSEMIDE	2 mL	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 34
HEPARIN	1 mL	OTHER: Q8HRS	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 34
FLUCONAZOLE	200 mg	OTHER: Q 24HOURS	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 43
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 43
METRONIDAZOLE	500 mg	OTHER: Q8HRS	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 43
GABAPENTIN	300 mg	TID	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 60
HYDROCODONE	325-5 mg	OTHER: Q6HR	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 60

METOPROLOL	0.5 mg	BID	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 60
ONDANSETRON	4 mg	OTHER: Q8HRS	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 60
OXYCODONE	5/325 mg	OTHER: 2 TABS Q4HR	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 60
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 60
POTASSIUM	20 mEq	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 60
SODIUM CHLORIDE	10 mL	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 60
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 60

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

Event Description	SMALL BOWEL OBSTRUCTION
Preferred term	小腸閉塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 8 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 26): Alanine Aminotransferase: 93 [Not reported - Not reported] Unit not reported; Albumin: 3.0 [Not reported - Not reported] Unit not reported; Alkaline Phosphatase: 74 [Not reported - Not reported] Unit not reported; Aspartate Aminotransferase: 46 [Not reported - Not reported] Unit not reported; Bilirubin: 0.7 [Not reported - Not reported] Unit not reported; Blood Urea Nitrogen: 9 [Not reported - Not reported] Unit not reported; Calcium: 9.4 [Not reported - Not reported] Unit not reported; Chloride: 102 [Not reported - Not reported] Unit not reported; Creatinine: 0.40 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Hemoglobin: 31.3 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Volume: 100.0 [Not reported - Not reported] Unit not reported; Erythrocytes: 3.87 [Not reported - Not reported] Unit not reported; Glucose: 87 [Not reported - Not reported] Unit not reported; Hematocrit: 38.7 [Not reported - Not reported] Unit not reported; Hemoglobin: 12.1 [Not reported - Not reported] Unit not reported; Leukocytes: 48.70 [Not reported - Not reported] Unit not reported; NPTST066-CO2: 30 [Not reported - Not reported] Unit not reported; NPTST152-LACTIC ACID: 6.3 [Not reported - Not reported] Unit not reported; Platelets: 461 [Not reported - Not reported] Unit not reported; Potassium: 5.7 [Not reported - Not reported] Unit not reported; Sodium: 141 [Not reported - Not reported] Unit not reported; [redacted]20[redacted] (Rx Day 34): Basophils: 0.03 [Not reported - Not reported] Unit not reported; Basophils/Leukocytes: 0.2 [Not reported - Not reported] Unit not reported; Blood Urea Nitrogen: 9 [Not reported - Not reported] Unit not reported; Calcium: 7.9 [Not reported - Not reported] Unit not reported; Chloride: 102 [Not reported - Not reported] Unit not reported; Creatinine: 0.30 [Not reported - Not reported] Unit not reported; Eosinophils: 0.02 [Not reported - Not reported] Unit not reported; Eosinophils/Leukocytes: 0.1 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Hemoglobin: 30.0 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Volume: 97.3 [Not reported - Not reported] Unit not reported; Erythrocytes: 2.93 [Not reported - Not reported] Unit not reported; Glucose: 103 [Not reported - Not reported] Unit not reported; Hematocrit: 28.5 [Not reported - Not reported] Unit not reported; Hemoglobin: 8.8 [Not reported - Not reported] Unit not reported; Leukocytes: 18.74 [Not reported - Not reported] Unit not reported; Lymphocytes: 0.61 [Not reported - Not reported] Unit not reported; Lymphocytes/Leukocytes: 3.3 [Not reported - Not reported] Unit not reported; Monocytes: 0.78 [Not reported - Not reported] Unit not reported; Monocytes/Leukocytes: 4.2 [Not reported - Not reported] Unit not reported; NPTST066-CO2: 33 [Not reported - Not reported] Unit not reported; NPTST165-MAGNESIUM: 2.0 [Not reported - Not reported] Unit not reported; NPTST194-PHOSPHATE: 2.8 [Not reported - Not reported] Unit

not reported; Neutrophils: 17.20 [Not reported - Not reported] Unit not reported; Neutrophils/Leukocytes: 91.7 [Not reported - Not reported] Unit not reported; Platelets: 452 [Not reported - Not reported] Unit not reported; Potassium: 4.1 [Not reported - Not reported] Unit not reported; Sodium: 142 [Not reported - Not reported] Unit not reported; [redacted]20[redacted] (Rx Day 35): Blood Urea Nitrogen: 10 [Not reported - Not reported] Unit not reported; Calcium: 7.8 [Not reported - Not reported] Unit not reported; Chloride: 100 [Not reported - Not reported] Unit not reported; Creatinine: 0.30 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Hemoglobin: 30.0 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Volume: 98.6 [Not reported - Not reported] Unit not reported; Erythrocytes: 2.80 [Not reported - Not reported] Unit not reported; Glucose: 104 [Not reported - Not reported] Unit not reported; Hematocrit: 27.6 [Not reported - Not reported] Unit not reported; Hemoglobin: 8.4 [Not reported - Not reported] Unit not reported; Leukocytes: 20.02 [Not reported - Not reported] Unit not reported; NPTST066-CO2: 31 [Not reported - Not reported] Unit not reported; Platelets: 447 [Not reported - Not reported] Unit not reported; Potassium: 3.9 [Not reported - Not reported] Unit not reported; Sodium: 136 [Not reported - Not reported] Unit not reported; [redacted]20[redacted] (Rx Day 36): Blood Urea Nitrogen: 8 [Not reported - Not reported] Unit not reported; Calcium: 7.8 [Not reported - Not reported] Unit not reported; Chloride: 98 [Not reported - Not reported] Unit not reported; Creatinine: 0.40 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Hemoglobin: 30.1 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Volume: 95.9 [Not reported - Not reported] Unit not reported; Erythrocytes: 2.69 [Not reported - Not reported] Unit not reported; Glucose: 94 [Not reported - Not reported] Unit not reported; Hematocrit: 25.8 [Not reported - Not reported] Unit not reported; Hemoglobin: 8.1 [Not reported - Not reported] Unit not reported; Leukocytes: 19.91 [Not reported - Not reported] Unit not reported; NPTST066-CO2: 30 [Not reported - Not reported] Unit not reported; NPTST165-MAGNESIUM: 1.9 [Not reported - Not reported] Unit not reported; NPTST194-PHOSPHATE: 2.8 [Not reported - Not reported] Unit not reported; Platelets: 452 [Not reported - Not reported] Unit not reported; Potassium: 4.0 [Not reported - Not reported] Unit not reported; Sodium: 134 [Not reported - Not reported] Unit not reported; [redacted]20[redacted] (Rx Day 37): Blood Urea Nitrogen: 6 [Not reported - Not reported] Unit not reported; Calcium: 7.9 [8.6169 - 10.0196] mg/dL; Chloride: 98 [Not reported - Not reported] Unit not reported; Creatinine: 0.30 [Not reported - Not reported] Unit not reported; Erythrocytes: 2.33 [Not reported - Not reported] Unit not reported; Glucose: 100 [Not reported - Not reported] Unit not reported; Hematocrit: 22.1 [39 - 49] %; Hemoglobin: 7.2 [Not reported - Not reported] Unit not reported; Leukocytes: 21.74 [Not reported - Not reported] Unit not reported; NPTST066-CO2: 32 [Not reported - Not reported] Unit not reported; Platelets: 427 [Not reported - Not reported] Unit not reported; Potassium: 3.8 [Not reported - Not reported] Unit not reported; Sodium: 135 [Not reported - Not reported] Unit not reported; [redacted]20[redacted] (Rx Day 38): Blood Urea Nitrogen: 4 [Not reported - Not reported] Unit not reported; Calcium: 7.8 [Not reported - Not reported] Unit not reported; Chloride: 97 [Not reported - Not reported] Unit not reported; Creatinine: 0.30 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Hemoglobin: 31.1 [Not reported - Not reported] Unit not reported; Ery. Mean Corpuscular Volume: 95.9 [Not reported - Not reported] Unit not reported; Erythrocytes: 2.70 [Not reported - Not reported] Unit not reported; Glucose: 94 [Not reported - Not reported] Unit not reported; He

Microbiology

[redacted]20[redacted] (Rx Day 40): OTHER ABDOMINAL ABSCESS NPTST104-FLUID CULTURE: POSITIVE-GRAM-POSITIVE COCCI AND 3+ YEASTS, ALSO SOME GRAM-NEGATIVE RODS

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 2): COLOSTOMY WITH ILEOCECECTOMY: COLECTOMY; CT ABDOMEN/PELVIS: MARKEDLY DILATED FLUID-FILLED SMALL BOWEL LOOPS PRESENT, MEASURING UP TO 8.8 CM WITH WALL THICKENING, MILD COLONIC DEBRIS, NO FREE AIR.; CT ABDOMEN/PELVIS: SEVERE GASTRIC DISTENTION WITH NUMEROUS DILATED SMALL BOWEL LOOPS WITH ASSOCIATED AIR-FLUID LEVELS. MOST CONSISTENT WITH SMALL BOWEL OBSTRUCTION. SMALL AMOUNT OF FREE INTRAPERITONEAL AIR, MODERATE FREE ABDOMINAL AND PELVIC FLUID. SMALL BILATERAL PLEURAL EFFUSIONS WITH DEPENDENT BILATERAL LOWER LOBE ATELECTASIS.; EXPLORATORY LAPAROTOMY: LYSIS OF ADHESIONS, REDUCTION AND CLOSURE OF INTERNAL HERNIA, SMALL BOWEL RESECTION PRIMARY ANASTOMOSIS; [redacted]20[redacted] (Rx Day 33): CT ABDOMEN/PELVIS: VERY LARGE

LOCULATED COLLECTION OF FLUID AND AIR IN THE ABDOMEN AND PELVIS, SUSPICIOUS FOR ABSCESS.; CT GUIDED FLUID DRAINAGE OF PERITONEAL ABSCESS: SUCCESSFUL CT-GUIDED 16 FRENCH DRAIN PLACEMENT WITHIN MID ABDOMINAL FLUID COLLECTION. A TOTAL OF 1000 ML OF PURULENT MATERIAL WAS ASPIRATED PRIOR TO ATTACHING DRAINAGE CATHETER TO BAG.; EXPLORATORY LAPAROTOMY: DRAINAGE OF FECULENT PERITONITIS ABDOMINAL WASHOUT, MASSIVE EXTENSIVE SEVERE LYSIS OF ADHESIONS, RESECTION OF PRIOR FAILED SMALL BOWEL ANASTOMOSIS WITH PRIMARY ANASTOMOSIS; US GUIDED THORACENTESIS: SUCCESSFUL ULTRASOUND GUIDED THORACENTESIS WITHIN THE LEFT CHEST WITH REMOVAL OF 1000 ML OF PLEURAL FLUID.

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	DISEASE EXACERBATION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	ABDOMINAL ABSCESS
Preferred term	腹部膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 40 (39 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	
Not Applicable	
Microbiology	
Not Applicable	
SAE Supplemental Procedure	
Not Applicable	
AE Stopped Rx Day	60 (59 DAYS AFTER LAST TREATMENT)
Duration of AE	21 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	Not Applicable
Discontinued Study Drug Due to the Event	YES
SAE Criteria	None

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

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

Event 1の臨床経過：

関連する病歴は，消化性潰瘍，クローン病，小腸結腸瘻，胃潰瘍，元喫煙者（1日2本を2年間），元喫煙者（電子タバコ1日2回を1年間未満）及び元飲酒者（2杯未満）であった。

投与8日後，被験者は小腸閉塞を発現した。

投与9日後，被験者は6ヵ月間で50ポンドの体重減少を報告し，食後の膨満感，悪心及び嘔吐を伴う心窩部苦悶を訴え救急科を受診した。被験者は1日に2～6回の軟らかく有形の排便があったと報告した。被験者によると，下痢や便中の粘液，膿，血液はなかった。投与17日後，被験者は試験開腹及び癒着の溶解，並びに小腸切除及び一期的吻合による内ヘルニアの整復と縫合を受けた。術後の固形食開始時に，被験者は腹部膨満及び疼痛の増加を発現した。CTスキャンが行われ，小腸閉塞に一致する重度の胃膨満，多数の拡張した小腸ループ及び関連する鏡面像が認められた。早期敗血症を考慮し，被験者はより綿密なケア及び観察の目的でICUに移送された。経験的抗生剤療法（詳細不明）の投与が開始され，経鼻胃管が留置された。投与40日後，CTスキャンが行われ，腹部及び骨盤部に大量の限局性の体液及び空気貯留が認められ，膿瘍が疑われた。その後CTガイド下で約1000 mLの膿性物質のドレナージが行われ，抗生剤療法は継続された。投与44日後，被験者は試験開腹のため再手術を受け，化膿性腹膜炎のドレナージ，腹部洗浄，広範囲で拡張性の癒着の重度溶解及び前回失敗した小腸吻合の切除術も行われた。術後，被験者は回復し，合併症は認められなかった。投与59日後，被験者は退院した。

本事象により治験薬の投与が完全に中止された。

投与された薬剤は，レボフロキサシン，メトロニダゾール，フルコナゾール，ガバペンチン，メトプロロール，パントプラゾール，hydrocodone，オキシコドン，オンダンセトロン，塩化ナトリウム，ヘパリン，フロセミド及び塩化カリウムであった。

The patient’s past medications include:

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

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

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

Causality for RISANKIZUMAB (Blinded)

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1) Small bowel obstruction (10041055) (Small intestinal obstruction (10041101)) [v.23.1] [10041055]

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 SMALL BOWEL OBSTRUCTION

- Investigator: disease exacerbation

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 93 (no units)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 8 (no units)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 10 (no units)

[redacted] 20[redacted] ALBUMIN: 3.0 (no units)

[redacted] 20[redacted] ALBUMIN: 2.1 (no units)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 74 (no units)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 68 (no units)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 91 (no units)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 46 (no units)

[redacted] 20[redacted] ASPARTATE AMINO TRANSFERASE: 22 (no units)

[redacted] 20[redacted] BILIRUBIN: 0.7 (no units)

[redacted] 20[redacted] BILIRUBIN: 0.1 (no units)

[redacted] **20[redacted] BUN:** 9 (no units)

[redacted] **20[redacted] BUN:** 3 (no units)

[redacted] **20[redacted] BUN:** 3 (no units)

[redacted] **20[redacted] BUN:** 4 (no units)

[redacted] 20[redacted] CALCIUM: 9.4 (no units)

[redacted] 20[redacted] CALCIUM: 7.6 G/DL

[redacted] 20[redacted] CALCIUM: 7.9 mg/dL

[redacted] 20[redacted] CALCIUM: 7.7 (no units)

[redacted] 20[redacted] CARBON DIOXIDE: 30 (no units)

[redacted] 20[redacted] CARBON DIOXIDE: 30 (no units)

[redacted] 20[redacted] CARBON DIOXIDE: 32 (no units)

[redacted] 20[redacted] CHLORIDE: 102 (no units)

[redacted] 20[redacted] CHLORIDE: 95 (no units)

[redacted] 20[redacted] CHLORIDE: 95 (no units)

[redacted] 20[redacted] CHLORIDE: 100 (no units)

[redacted] 20[redacted] CREATININE: 0.40 (no units)

[redacted] 20[redacted] CREATININE: 0.30 (no units)

[redacted] 20[redacted] CREATININE: 0.40 (no units)

[redacted] 20[redacted] CREATININE: 2.4 (no units)

[redacted] 20[redacted] CREATININE: 0.40 (no units)

[redacted] **20[redacted] CT ABDOMEN PELVIS:** Markedly dilated fluid-filled small bowel loops present, measuring up to 8.8 cm with wall-thickening mild colonic debris, no free air.

[redacted] **20[redacted] CT ABDOMEN PELVIS:** Severe gastric distention with numerous dilated small bowel loops with associated air-fluid levels. Most consistent with small bowel obstruction. Small amount of free intraperitoneal air, moderate free abdominal and pelvic fluid. Small bilateral pleural effusions with dependent bilateral lower lobe atelectasis.

[redacted] **20[redacted] CT ABDOMEN PELVIS:** Very large loculated collection of fluid and air in the abdomen and pelvis, suspicious for abscess.

[redacted] **20[redacted] CULTURE:** Abdominal abscess fluid: positive for gram-positive cocci and 3+ yeasts, also some gram-negative rods.

[redacted] 20[redacted] GLUCOSE: 87 (no units)

[redacted] 20[redacted] GLUCOSE: 125 (no units)

[redacted] 20[redacted] GLUCOSE: 120 (no units)

[redacted] 20[redacted] GLUCOSE: 125 (no units)

[redacted] 20[redacted] GLUCOSE: 75 (no units)

[redacted] 20[redacted] GLUCOSE: 129 (no units)

[redacted] 20[redacted] HCT: 38.7 %

[redacted] 20[redacted] HCT: 22.8 %

[redacted] 20[redacted] HCT: 25.6 %

[redacted] 20[redacted] HCT: 21.4 %

[redacted] 20[redacted] HCT: 25.8 %

[redacted] 20[redacted] HGB: 12.1 G/DL

[redacted] 20[redacted] HGB: 7.1 G/DL

[redacted] **20[redacted] HGB:** 8.0 (no units)

[redacted] 20[redacted] HGB: 6.8 G/DL

[redacted] 20[redacted] HGB: 8.7 G/DL

[redacted] 20[redacted] LACTIC ACID: 6.3 (no units)

[redacted] 20[redacted] MAGNESIUM: 1.8 (no units)

[redacted] **20[redacted] MCH:** 31.3 (no units)

[redacted] **20[redacted] MCH:** 29.3 (no units)

[redacted] **20[redacted] MCH:** 29.2 (no units)

[redacted] **20[redacted] MCV:** 100.0 (no units)

[redacted] **20[redacted] MCV:** 93.4 (no units)

[redacted] 20[redacted] MCV: 93.8 G/DL

[redacted] **20[redacted] MCV:** 91.8 (no units)

[redacted] **20[redacted] MCV:** 90.2 (no units)

[redacted] 20[redacted] OCCULT BLOOD: 33 (no units)

[redacted] 20[redacted] PHOSPHATE: 3.9 (no units)

[redacted] 20[redacted] PLATELET COUNT: 461 (no units)

[redacted] 20[redacted] PLATELET COUNT: 654 (no units)

[redacted] 20[redacted] PLATELET COUNT: 692 (no units)

[redacted] 20[redacted] PLATELET COUNT: 579 (no units)

[redacted] 20[redacted] POTASSIUM: 5.7 (no units)

[redacted] 20[redacted] POTASSIUM: 3.7 (no units)

[redacted] 20[redacted] POTASSIUM: 3.3 (no units)

[redacted] 20[redacted] POTASSIUM: 4.0 (no units)

[redacted] **20[redacted] RBC:** 3.87 (no units)

[redacted] **20[redacted] RBC:** 2.44 (no units)

[redacted] **20[redacted] RBC:** 2.73 (no units)

[redacted] **20[redacted] RBC:** 2.33 (no units)

[redacted] **20[redacted] RBC:** 2.86 (no units)

[redacted] 20[redacted] SODIUM: 141 (no units)

[redacted] 20[redacted] SODIUM: 135 (no units)

[redacted] 20[redacted] SODIUM: 135 (no units)

[redacted] 20[redacted] SODIUM: 136 (no units)

[redacted] **20[redacted] WBC:** 48.70 (no units)

[redacted] **20[redacted] WBC:** 12.03 (no units)

[redacted] **20[redacted] WBC:** 9.18 (no units)

[redacted] **20[redacted] WBC:** 5.90 (no units)

[redacted] **20[redacted] WBC:** 9.93 (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
胃腸出血	X			

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

Medical History	Onset Year
OTHER: ETHANOL ABUSE	19[redacted]
MYOCARDIAL INFARCTION	20[redacted]
OTHER: HYPERCHOLESTEROLEMIA	20[redacted]
OTHER: DYSPHAGIA	20[redacted]
OTHER: SLEEP APNEA	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20[redacted]
OTHER: ESOPHAGEAL STRICTURE	20[redacted]
OTHER: KIENBOCKS DISESE RIGHT WRIST	20[redacted]
CROHN'S DISEASE	20[redacted]

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

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CIGARETTES	FORMER	20 CIGARETTE	1.5	19[redacted]
CHEWING TOBACCO	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2 - 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 62	62
Risankizumab	1200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 83	[redacted]20[redacted] / 134	52

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ASCORBIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -311
FISH OIL	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / -311
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted] / -311
VITAMIN D NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -311
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -311
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -228
MESALAZINE	1000 mg	BID	Y-M: 20[redacted] / -189
MELOXICAM	150 mg	QD	Y-M: 20[redacted] / -49
MAGNESIUM CITRATE	10 OTHER: OUNCES	OTHER: ONE TIME DOSE	Y-M: 20[redacted] / -20
GOLYTELY	4 OTHER: LITERS	QD	Y-M: 20[redacted] / -19
PROPOFOL	400 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / -18
HEPATITIS A VACCINE	1 mL	OTHER: INJECTIONS	Y-M: 20[redacted] / -10

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
ASCORBIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -311	ONGOING
FISH OIL	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / -311	ONGOING
VITAMIN D NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -311	ONGOING
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -311	ONGOING
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted] / -311	Y-M: 20[redacted] / 17
MESALAZINE	1000 mg	BID	Y-M: 20[redacted] / -189	ONGOING
MELOXICAM	150 mg	QD	Y-M: 20[redacted] / -49	Y-M: 20[redacted] / 17
HEPATITIS A VACCINE	1 mL	OTHER: INJECTIONS	Y-M: 20[redacted] / -10	ONGOING
FAMOTIDINE	20 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 17
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 17
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 19	ONGOING

Event #1: Serious Adverse Event

Event Description	GASTROINTESTINAL HEMORRHAGE

Preferred term	胃腸出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 15
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 17): Hematocrit: 30.4 [38 - 50] %; Hemoglobin: 10.8 [13.5 - 17.5] g/dL

Microbiology

[redacted]20[redacted] (Rx Day 17): STOOL NPTST184-OCCULT BLOOD: POSITIVE-POSITIVE

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day -7): CT ABDOMEN AND PELVIS: A SMALL HIATAL HERNIA IS SEEN, THERE ARE DIVERTICULA SCATTERED THROUGHOUT THE LARGE BOWEL. THERE IS NO DEFINITE EVIDENCE OF DIVERTICULITIS. A DISTAL TERMINAL ILEUM AND CECUM HAVE FAT WITHIN THE WALL WHICH IS MOST LIKELY SECONDARY TO CROHN'S DISEASE. NO DEFINITE ACTIVE CROHN'S DISEASE IS SEEN.; ESOPHAGOGASTRODUODENOSCOPY WITH DIALATION.: DISTAL ESOPHAGEAL RING WITH 48 FR SAVORY DIALATION. HIATAL HERNIA AND ANTRAL EROSIONS

AE Stopped Rx Day	19
Duration of AE	5 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	HISTORY OF CROHN'S DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

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

Event 1 の臨床経過：

関連する病歴は，元喫煙者（1 日 20 本を 1.5 年間），心筋梗塞，嚥下障害，胃食道逆流性疾患，食道狭窄，クローン病及び飲酒者（1 日 2～4 杯）であった。

投与 15 日後，被験者は胃腸出血を発現した。投与 19 日後，胃腸出血は消失した。

投与 17 日後，被験者は 3 日間にわたる黒色タール様便及び腹痛のため入院した。被験者は IV プロトンポンプ阻害剤及び IV 補液による治療を受けた。入院中の合併症は報告されなかった。投与 19 日後，被験者は退院した。

被験者はアルコール乱用の病歴があり，飲酒を継続している。被験者は胃腸出血の既往歴はないと述べた。

投与された薬剤は，Pepcid 及び塩化ナトリウムであった。

Causality for RISANKIZUMAB (Blinded)

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1) Gastrointestinal hemorrhage (10017960) (Gastrointestinal haemorrhage (10017955)) [v.23.0] [10017960]

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 GASTROINTESTINAL HEMORRHAGE

- Investigator: History of Crohn's Disease

- AbbVie: Event more likely related to pre-existing Crohn's Disease, chronic and on-going alcohol consumption.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** A small hiatal hernia is seen, there are diverticula scattered throughout the large bowel. There is no definite evidence of diverticulitis. A distal terminal ileum and cecum have fat within the wall which is most likely secondary to Crohn's disease. No definite active Crohn's disease is seen.

[redacted] **20[redacted] ESOPHAGOGASTRODUODENOSCOPY:** Distal esophageal ring with 48 Fr savory dialation. Hiatal hernia and antral erosions

[redacted] **20[redacted] HEMATOCRIT:** 30.4 % (normal 38 to 50)

[redacted] **20[redacted] HEMOGLOBIN:** 10.8 G/DL (normal 13.5 to 17.5)

[redacted] 20[redacted] OCCULT BLOOD IN STOOL: Positive

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:RZB 600 MG IV / P2:RZB 1200 MG IV	7[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: HYSTERECTOMY	19[redacted]
OTHER: SEASONAL ALLERGIES	19[redacted]
ANEMIA: IRON DEFICIENCY	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: INTERMITTENT ABDOMINAL PAIN	20[redacted]
OTHER: INTERMITTENT DIARRHEA	20[redacted]
HYPERLIPIDEMIA: HIGH CHOLESTEROL	20[redacted]
HYPOTHYROIDISM	20[redacted]
OTHER: SIGMOID DILATION	20[redacted]
OTHER: SIGMOID STRICTURE	20[redacted]
OTHER: HIGH CHOLESTEROL	20[redacted]
OTHER: RECURRENT CDIFF INFECTION	20[redacted]
OTHER: INTERMITTENT CHILLS	20[redacted]
OTHER: INTERMITTENT FATIGUE	20[redacted]
OTHER: INTERMITTENT FECAL INCONTINENCE	20[redacted]
OTHER: INTERMITTENT MALAISE	20[redacted]
OTHER: INTERMITTENT NIGHT SWEATS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	19[redacted]
SURGERY: APPENDECTOMY	19[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
SURGERY: RESECTION OF ENTEROCOLONIC FISTULA	20[redacted]
SURGERY: SIGMOID COLECTOMY WITH ILEOCOLONIC RESECTION	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

E-CIGARETTES	NEVER
PIPES	NEVER

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	600 mg	IV	Every 4 Weeks	[redacted] / 1	[redacted] / 57	57
Risankizumab	1200 mg	IV	Every 4 Weeks	[redacted] / 100	[redacted] / 142	43

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
DIPHENHYDRAMINE	25 mg	PRN	Y-M: 19[redacted]
MERCAPTOPURINE	50 mg	QD	Y-M: 20[redacted]
MESALAZINE	1.5 g	QD	Y-M: 20[redacted]
LEVOTHYROXINE	112 ug	QD	Y-M: 20[redacted]
MESALAZINE	1.5 g	QD	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: Q8WEEKS	Y-M: 20[redacted]
GUSELKUMAB	200 mg	OTHER: ONCE	Y-M: 20[redacted] / -105
PRENATAL VITAMINS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -35
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -26
SUPREP BOWEL PREP	1 OTHER: KIT	OTHER: ONCE	Y-M: 20[redacted] / -15
PROPOFOL	300 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / -14

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
DIPHENHYDRAMINE	25 mg	PRN	Y-M: 19[redacted]	ONGOING
LEVOTHYROXINE	112 ug	QD	Y-M: 20[redacted]	ONGOING
PRENATAL VITAMINS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -35	ONGOING
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -26	Y-M: 20[redacted] / 100
HYDROMORPHONE	0.2-0.4 mg	PRN	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
CIPROFLOXACIN	200 mg	OTHER: Q12HRS	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 86
METOCLOPRAMIDE	5 mg	OTHER: Q6HRS	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 86
METRONIDAZOLE	500 mg	OTHER: Q8HRS	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 86

PARACETAMOL	803 mg	OTHER: Q6HRS	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 86
HYDROMORPHONE	0.5 OTHER: MG/ML	PRN	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 90

Event #1: Serious Adverse Event

Event Description	COLON PERFORATION
Preferred term	大腸穿孔
AE Onset Date / Rx Day	[redacted]20[redacted] / 85
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 85): Albumin: 3.0 [3.9 - 5] Unit not reported; Alkaline Phosphatase: 77 [38 - 126] IU/L; Bilirubin: 0.3 [0.2 - 1.3] mg/dL; Blood Urea Nitrogen: 29 [7 - 17] mg/dL; Calcium: 9.0 [8.4 - 10.2] mg/dL; Chloride: 97 [100 - 108] mmol/L; Creatinine: 1.31 [0.5 - 1.4] mg/dL; Ery. Mean Corpuscular Hemoglobin: 24.7 [26 - 34] pg; Ery. Mean Corpuscular Volume: 78.3 [79.3 - 94.8] Unit not reported; Erythrocytes: 3.31 [4 - 5.2] Unit not reported; Glucose: 123 [70 - 110] mg/dL; Hematocrit: 25.9 [36 - 46] %; Hemoglobin: 8.2 [12 - 16] Unit not reported; Leukocytes: 4.0 [4.5 - 11] 10^3/uL; Lipase: 12 [23 - 300] IU/L; NPTST011-ALT: 15 [0 - 35] IU/L; NPTST013-ANION GAP: 15 [8 - 16] mmol/L; NPTST014-ANISOCYTOSIS: 3+ [Not reported - Not reported] Unit not reported; NPTST025-AST: 24 [14 - 36] IU/L; NPTST036-BASOPHILS RELATIVE: 1 [0 - 2] %; NPTST047-BUN/CREATINE RATION: 22 [12 - 20] RATIO; NPTST068-CO2 BICARBONATE: 19.3 [22 - 30] mmol/L; NPTST088-EOSINOPHILS RELATIVE: 0 [0 - 5] %; NPTST113-GFR MDRD NO: 39 [60 - 60] Unit not reported; NPTST159-LYMPHOCYTE RELATIVE: 13 [22 - 44] %; NPTST161-LYMPHOCYTES ABSOLUTE: 0.5 [1 - 4.8] 10^3/uL; NPTST167-MCHC: 31.6 [31 - 37] Unit not reported; NPTST175-MONOCYTES ABSOLUTE: 0.6 [0 - 1.1] 10^3/uL; NPTST176-MONOCYTES RELATIVE: 14 [0 - 10] %; NPTST177-MPV: 7.0 [7.5 - 10.7] Unit not reported; NPTST185-OSMOLALITY CALC: 269 [275 - 295] Unit not reported; NPTST215-RDW: 23.1 [11.5 - 14.5] %; NPTST240-SEGS: 72 [36 - 66] %; NPTST241-SEGS ABSOLUTE: 2.9 [1.8 - 7.8] 10^3/uL; Platelets: 554 [150 - 450] 10^3/uL; Potassium: 4.1 [3.5 - 5.3] mmol/L; Protein: 6.5 [6.3 - 8.2] Unit not reported; Sodium: 131 [137 - 145] mmol/L; [redacted]20[redacted] (Rx Day 86): Blood Urea Nitrogen: 27 [7 - 17] mg/dL; Calcium: 7.6 [8.4 - 10.2] mg/dL; Chloride: 104 [100 - 108] mmol/L; Creatinine: .97 [0.5 - 1.4] mg/dL; Ery. Mean Corpuscular Hemoglobin: 25.6 [26 - 34] pg; Ery. Mean Corpuscular Volume: 77.8 [79.3 - 94.8] fL; Erythrocytes: 4.08 [4 - 5.2] Unit not reported; Glucose: 155 [70 - 110] mg/dL; Hematocrit: 31.7 [36 - 46] %; Hemoglobin: 10.4 [12 - 16] Unit not reported; Leukocytes: 9.7 [4.5 - 11] 10^3/uL; Lymphocytes: .4 [1 - 4.8] 10^3/uL; Monocytes: .7 [0 - 1.1] 10^3/uL; NPTST013-ANION GAP: 7 [8 - 16] mmol/L; NPTST014-ANISOCYTOSIS: 2+ [Not reported - Not reported] Unit not reported; NPTST036-BASOPHILS RELATIVE: 0 [0 - 2] %; NPTST048-BUN/CREATININE RATIO: 28 [12 - 20] RATIO; NPTST067-CO2 - BICARBONATE: 20 [22 - 30] mmol/L; NPTST088-EOSINOPHILS RELATIVE: 0 [0 - 5] %; NPTST112-GFR MDRD AF AMER: 67 [60 - Not reported] Unit not reported; NPTST114-GFR MDRD NON AF AMER: 56 [60 - Not reported] Unit not reported; NPTST162-LYMPHOCYTES RELATIVE: 4 [24 - 44] %; NPTST167-MCHC: 32.9 [31 - 37] Unit not reported; NPTST176-MONOCYTES RELATIVE: 7 [0 - 10] %; NPTST177-MPV: 7.7 [7.5 - 10.7] Unit not reported; NPTST185-OSMOLALITY CALC: 271 [275 - 295] Unit not reported; NPTST215-RDW: 21 [11.5 - 14.5] %; NPTST241-SEGS ABSOLUTE: 8.6 [1.8 - 7.7] 10^3/uL; NPTST242-SEGS RELATIVE: 88 [36 - 66] %; Platelets: 464 [150 - 450] 10^3/uL; Potassium: 4.4 [3.5 - 5.3] mmol/L; Sodium: 131 [137 - 145] mmol/L; [redacted]20[redacted] (Rx Day 88): Alanine Aminotransferase: 14 [0 - 35] IU/L; Albumin: 2 [3.9 - 5] Unit not reported; Alkaline Phosphatase: 82 [38 - 126] IU/L; Aspartate Aminotransferase: 20 [14 - 36] IU/L; Bilirubin: .4 [0.2 - 1.3] mg/dL; Blood Urea Nitrogen: 10 [7 - 17] mg/dL; Calcium: 7.9 [8.4 - 10.2] mg/dL; Chloride: 113 [100 - 108] mmol/L; Creatinine: .69 [0.5 - 1.4] mg/dL; Eosinophils: .3 [0 - 0.7] 10^3/uL; Ery. Mean Corpuscular Hemoglobin: 25.6 [26 - 34] pg; Ery. Mean Corpuscular Volume: 80.9 [79.3 - 94.8] fL; Erythrocytes: 3.96 [4 - 5.2] Unit not reported; Glucose: 117 [70 - 110] mg/dL; Hematocrit: 32 [36 - 46] %; Hemoglobin: 10.1 [12 - 16] Unit not reported; Leukocytes: 14.9 [4.5 - 11] 10^3/uL; Lymphocytes: .9 [1 - 4.8] 10^3/uL; Monocytes: .6 [0 - 1.1] 10^3/uL; NPTST009-

ALBUMIN/GLOBULIN RATIO: .7 [1.1 - 2] RATIO; NPTST013-ANION GAP: 4 [8 - 16] mmol/L; NPTST014-ANISOCYTOSIS: 2+ [Not reported - Not reported] Unit not reported; NPTST036-BASOPHILS RELATIVE: 0 [0 - 2] %; NPTST048-BUN/CREATININE RATIO: 14 [12 - 20] RATIO; NPTST067-CO2 - BICARBONATE: 19 [22 - 30] mmol/L; NPTST088-EOSINOPHILS RELATIVE: 2 [0 - 5] %; NPTST112-GFR MDRD AF AMER: 100 [60 - Not reported] Unit not reported; NPTST114-GFR MDRD NON AF AMER: 82 [60 - Not reported] Unit not reported; NPTST162-LYMPHOCYTES RELATIVE: 6 [24 - 44] %; NPTST167-MCHC: 31.6 [31 - 37] Unit not reported; NPTST176-MONOCYTES RELATIVE: 4 [0 - 10] %; NPTST177-MPV: 7.3 [7.5 - 10.7] Unit not reported; NPTST185-OSMOLALITY CALC: 272 [275 - 295] Unit not reported; NPTST215-RDW: 21.3 [11.5 - 14.5] %; NPTST241-SEGS ABSOLUTE: 13.1 [1.8 - 7.7] 10^3/uL; NPTST242-SEGS RELATIVE: 88 [36 - 66] %; Platelets: 425 [150 - 450] 10^3/uL; Potassium: 5 [3.5 - 5.3] mmol/L; Protein: 4.7 [6.3 - 8.2] Unit not reported; Sodium: 136 [137 - 145] mmol/L

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 57): EXPLORATORY LAPAROTOMY WITH PROCTOSIGMOIDOSCOPY: SUBJECT HAD A TAKEDOWN OF THE SPLENIC FLEXURE, SEGMENTAL RESECTION LEFT TRANSVERSE COLON WITH ISOPERISTALTIC COLO-COLIC ANASTOMOSIS; TRANSVERSE COLON SEGMENTAL RESECTION: DISCHARGE CONDITION, GOOD

AE Stopped Rx Day	85
Duration of AE	1 DAY
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	BOWEL PERFORATION DURING PROCEDURE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

米国の治験責任医師からの報告。本被験者は 7[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，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，腸切除，小腸結腸瘻切除，S 状結腸切除及び回腸結腸切除，非喫煙者，並びに飲酒者（1 日 2 杯未満）であった。

投与 85 日後，被験者は結腸穿孔を発現した。投与 85 日後，結腸穿孔は消失した。

本事象発現前の投与開始当月，被験者は感染性大腸炎（非重篤）を発現した。

投与 85 日後，被験者は結腸内視鏡検査を受けた。被験者には左下腹部（LLQ）の腹痛の増加及び限局性腹膜炎があった。検査時，肛門縁から 35 cm の位置に高度狭窄があり，結腸内視鏡の通過を阻んでいた。ガイドワイヤーが留置され，拡張が行われた。内視鏡の再挿入時，全層性の穿孔の証拠が認められた。検査は中断され，被験者は根本的外科治療の目的で当院に救急搬送された。被験者は横行結腸部分切除，並びに試験正中線開腹及び直腸 S 状結腸鏡検査を受けた。被験者は脾湾曲部摘出，部分切除，並びに左横行結腸及び順蠕動結腸吻合を受けた。腹腔内癒着が広範囲に認められた。穿孔部位は左横行結腸に位置しており，クローン病に一致する慢性穿孔の徴候を示していた。吻合を伴う一次切除を完了した。術後，消化管機能が回復し消化液が徐々に産出されるまで経鼻胃管が 48 時間使用された。最終的な病理はクローン病と一致していた。投与 91 日後，被験者は良好な状態で退院した。

投与された薬剤は，ヒドロモルフォン，塩化ナトリウム，メトクロプラミド，メトロニダゾール，ガバペンチン，Ofirmev，Lovenox，Cipro，タイレノール，パントプラゾール及びピペラシリン-タゾバクタムであった。

The patient’s past medications include:

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

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

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

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

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

CIPROFLOXACIN for INFECTIOUS COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FLAGYL for INFECTIOUS COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for RISANKIZUMAB (Blinded)

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1) Colon perforation (10009977) (Large intestine perforation (10023804)) [v.23.1] [10009977]

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 PERFORATION

- Investigator: Bowel perforation during procedure

- AbbVie: Event is more likely related to the colonoscopy procedure as noted by PI. Additional risk factor includes pre-existing crohn's disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 3.0 GM/DL (normal 3.9 to 5.0)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 77 IU/L (normal 38 to 126)

[redacted] 20[redacted] ALANINE TRANSAMINASE: 15 IU/L (normal 0 to 35)

[redacted] **20[redacted] AST:** 24 IU/L (normal 14 to 36)

[redacted] **20[redacted] BILIRUBIN:** 0.3 mg/dL (normal 0.2 to 1.3)

[redacted] **20[redacted] BUN:** 29 mg/dL (normal 7 to 17)

[redacted] **20[redacted] CHLORIDE:** 97 MMOL/L (normal 100 to 108)

[redacted] **20[redacted] CREATININE:** 1.31 mg/dL (normal 0.50 to 1.40)

[redacted] **20[redacted] GLUCOSE:** 123 mg/dL (normal 70 to 110)

[redacted] **20[redacted] HEMATOCRIT:** 25.9 % (normal 36.0 to 46.0)

[redacted] **20[redacted] HEMOGLOBIN:** 8.2 GM/DL (normal 12 to 16)

[redacted] 20[redacted] ILEOCOLONOSCOPY: not reported

[redacted] **20[redacted] LIPASE:** 12 IU/L (normal 23 to 300)

[redacted] **20[redacted] PLATELET:** 554 X10**3/MCL (normal 150 to 450)

[redacted] **20[redacted] POTASSIUM:** 4.1 MMOL/L (normal 3.5 to 5.3)

[redacted] **20[redacted] PROTEIN:** 6.5 GM/DL (normal 6.3 to 8.2)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.31 MIL/UL (normal 4.0 to 5.20)

[redacted] **20[redacted] SODIUM:** 131 MMOL/L (normal 137 to 145)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4.0 X10**3/MCL (normal 4.5 to 11.0)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO	2[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
OTHER: MORBID OBESITY	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: ACUTE APPENDICITIS	20[redacted]
OTHER: COMPLETE BOWEL OBSTRUCTION	20[redacted]
OTHER: RIGHT ABDOMINAL HERNIA	20[redacted]
OTHER: CONSTIPATION	20[redacted]
OTHER: HYPERTENSION PROPHYLAXSIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: LAPAROSCOPIC APPENDECTOMY	20[redacted]
CROHN'S DISEASE SURGICAL HISTORY: BOWEL RESECTION	20[redacted]
SURGERY: LAPAROSCOPIC-ASSISTED ILEOCECAL EXCISION AND ILEAL ASCENDING STAPLED ANASTOMOSIS	20[redacted]
CROHN'S DISEASE HISTORY: COLONOSCOPY	20[redacted]
ENDOSCOPY (SCREENING): BIOPSY	20[redacted]
ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44

Interruption	[redacted]20[redacted] / 45	[redacted]20[redacted] / 101	57	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
ADALIMUMAB	40 mg	OTHER: Q2WEEKS	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -64
BISACODYL	10 mg	QD	Y-M: 20[redacted] / -51
CLONIDINE	0.1 mg	TID	Y-M: 20[redacted] / -51
DIPHENHYDRAMINE	25 MG mg	QD	Y-M: 20[redacted] / -51
FAMOTIDINE	20 MG mg	QD	Y-M: 20[redacted] / -51
HYDRALAZINE	20 mg	OTHER: Q4H	Y-M: 20[redacted] / -51
MAGNESIUM HYDROXIDE	2.4 mg	QD	Y-M: 20[redacted] / -51
MORPHINE	2 mg	OTHER: Q4H	Y-M: 20[redacted] / -51
MYLANTA	30 ML mL	OTHER: Q4H	Y-M: 20[redacted] / -51
ONDANSETRON	4 MG mg	OTHER: Q6H	Y-M: 20[redacted] / -51
PARACETAMOL	650 MG mg	OTHER: Q4H	Y-M: 20[redacted] / -51
POTASSIUM	20 mEq	QD	Y-M: 20[redacted] / -51
PROMETHAZINE	25 MG mg	OTHER: Q8H	Y-M: 20[redacted] / -51
DOCUSATE	100 mg	QD	Y-M: 20[redacted] / -21
MACROGOL 3350	238 g	Not reported.	Y-M: 20[redacted] / -21

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
DIPHENHYDRAMINE	25 mg	PRN	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
IOPAMIDOL	100 mL	OTHER: ONLY DOSE	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
MORPHINE	2 mg	OTHER: ONE DOSE	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
ONDANSETRON	4 mg	OTHER: ONE DOSE	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
CEFTRIAXONE	1 g	QD	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 27
MORPHINE	2 mg	PRN	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 27
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 27

PIP/TAZO	3.375 g	OTHER: Q8H	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 27
ZOLPIDEM	5 mg	PRN	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 27
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / 36	ONGOING

Event #1: Serious Adverse Event

Event Description	WORSENING ADBOMINAL PAIN
Preferred term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 24
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 26): Hemoglobin: 11.7 [12 - 16] g/dL; Neutrophils/Leukocytes: 68.3 [36 - 66] %

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 24): CT SCAN ABDOMEN AND PELVIS W/CONTRAST: 1.DEVELOPMENT OF SMALL SUBPLEURAL NODULAR AIRSPACE DISEASE OR ROUNDED ATELECTASIAS IN THE RLL.2. RLQ HERNIA SAC CONTAINING UNOBSTRUCTED SMALL AND LARGE BOWEL. 3. CHOLELITHIASIS AND GALLBLADDER SLUDGE.; CXR: LOW LUNG VOLUMES WITH PERIHILAR CROWDING.

AE Stopped Rx Day	41
Duration of AE	18 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SUBJECT PRESENTED TO THE ER ON [redacted] WITH MODERATE ABDOMINAL PAIN AND ADMITTED FOR EVALUATION AND SHE WAS SUBSEQUENTLY FOUND TO BE COV-19 PCR POSITIVE AND GIVEN IV ANTIBIOTIC AND MORPHINE FOR PAIN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

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

Event 1 の臨床経過：

関連する病歴は，病的肥満，クローン病，完全腸閉塞，右腹部ヘルニア，便秘，非喫煙者及び禁酒であった。

投与 24 日後，被験者は腹痛悪化を発現した。投与 41 日後，腹痛悪化は消失した。

投与 26 日後，被験者は発熱，腹痛，悪心，嘔吐，倦怠感及び下痢のため入院した。被験者は CT スキャンを受け，結果は肺炎（非重篤）と一致していた。その後，被験者は COVID-19（非重篤）の検査結果が陽性であった。また，疼痛に対して抗生剤及びモルヒネが投与された。投与 27 日後，被験者は退院した。

投与された薬剤は，モルヒネ硫酸塩であった。

The patient’s past medications include:

HUMIRA for CROHN'S DISEASE ([redacted])

BUDESONIDE for CROHN'S DISEASE ([redacted])

MORPHINE for ABDOMINAL PAIN ([redacted])

MYLANTA for PROPHYLAXIS GASTRIC ULCERS ([redacted])

PEPCID for PROPHYLAXIS GASTRIC ULCERS ([redacted])

TYLENOL for CROHN'S DISEASE ([redacted])

Causality for RISANKIZUMAB (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of WORSENING ADBOMINAL PAIN

- **Investigator:** Patient presented to the ER on [redacted] with moderate abdominal pain and admitted for evaluation and she was subsequently found to be COVID-19 PCR positive and given IV ANTIBIOTIC and MORPHINE for pain.

- **AbbVie:** Risk factors include concurrent covid-19 infection, underlying crohn's disease and prior abdominal surgeries.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD PRESSURE: 134/71 mmHg

[redacted] 20[redacted] BODY TEMPERATURE: 102.6 F

[redacted] 20[redacted] COVID-19 STATUS BLOOD TEST: Positive

[redacted] **20[redacted] CT SCAN:** FINDINGS CONSISTENT WITH PNEUMONIA.

[redacted] **20[redacted] CT SCAN ABDOMEN AND PELVIS:** 1.Development of small subpleural nodular airspace disease or rounded atelectasias in the RLL.2. RLQ hernia sac containing unobstructed small and large bowel. 3. Cholelithiasis and gallbladder sludge.

[redacted]**020 CXR:** Low lung volumes with perihilar crowding.

[redacted] **20[redacted] HEMOGLOBIN:** 11.7 G/DL (normal 12 to 16)

[redacted] **20[redacted] NEUTROPHILS %:** 68.3 % (normal 36 to 66)

[redacted] 20[redacted] PULSE: 114 MIN

[redacted] 20[redacted] PULSE OX: 100 %

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

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

Medical History	Onset Year
OTHER: PERI-ANAL FISTULA	20[redacted]
ANEMIA: NORMOCHROMIC ANEMIA	20[redacted]
CROHN'S DISEASE	20[redacted]
OTHER: INTOLERANCE TO AZATHIOPRINE (IMUREL)	20[redacted]
OTHER: CYTOMEGALOVIRUS (CMV) COLONIC	20[redacted]
INFLAMMATORY BOWEL DISEASE: CROHN'S DISEASE FLARE	20[redacted]
OTHER: IRON DEFICIENCY	20[redacted]

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

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CIGARETTES	CURRENT	15 CIGARETTE	8	Not reported.
CHEWING TOBACCO	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
Risankizumab	1200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 89	[redacted]20[redacted] / 145	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
PARACETAMOL	650-1000 mg	PRN	Y-M: 20[redacted]
CALCIUM	500 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	1000 IU	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: QWEEKLY	Y-M: 20[redacted]
AZATHIOPRINE	Not reported.	QD	Y-M: 20[redacted]
USTEKINUMAB	90 mg	OTHER: Q4WEEKS	Y-M: 20[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -24
PREDNISONE	25 mg	QD	Y-M: 20[redacted] / -17
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -10
PICO-SALAX	1 OTHER: SACHET	OTHER: X 2 DOSES	Y-M: 20[redacted] / -9
MAGNESIUM CITRATE	150 mL	OTHER: ONCE	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
PARACETAMOL	650-1000 mg	PRN	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	1000 IU	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 71
CALCIUM	500 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 153
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -10	Y-M: 20[redacted] / 39
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 114
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 114
DIMENHYDRINATE	25 mg	OTHER: X1	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 35
POTASSIUM	40 mmol	OTHER: X1	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 35
EL-4	100 OTHER: ML/HR	OTHER: CONTINUOUS DRIP	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 36
MORPHINE	7.5 mg	PRN	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 36
METHYLPREDNISOLONE	20 mg	TID	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 40
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 42
IRON	200 mg	OTHER: Q 2 DAYS	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 38
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 39

DALTEPARIN	5000 OTHER: UNITS	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 40
HYDROMORPHONE	0.25 mg	PRN	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 41
SODIUM CHLORIDE	Not reported.	OTHER: CONTINUOUS	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 42
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 102
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 42

Event #1: Serious Adverse Event

Event Description	CROHN'S DISEASE EXACERBATION
Preferred term	クローン病
AE Onset Date / Rx Day	[redacted]20[redacted] / 35
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (Rx Day 35): Alanine Aminotransferase: 12 [6 - 45] U/L; Alkaline Phosphatase: 54 [53 - 128] U/L; Bilirubin: 10.0 [1.7 - 18.9] umol/L; Chloride: 95 [100 - 109] mmol/L; Creatinine: 85 [55 - 110] umol/L; Ery. Mean Corpuscular Volume: 73.7 [80 - 100] fL; Erythrocytes: 5.67 [4.5 - 5.9] 10^12/L; Hematocrit: 0.418 [0.42 - 0.52] Unit not reported; Hemoglobin: 135 [135 - 175] g/L; Leukocytes: 16.00 [4.5 - 11] 10^9/L; Lipase: 25 [14 - 45] U/L; Lymphocytes: 3.50 [1 - 4.8] 10^9/L; NPTST070-CRP: 48.43 [0 - 5] mg/L; Neutrophils: 10.84 [1.8 - 7.7] 10^9/L; Platelets: 457 [140 - 450] 10^9/L; Potassium: 3.2 [3.5 - 5] mmol/L; Sodium: 135 [133 - 143] mmol/L; [redacted]20[redacted] (Rx Day 36): Calcium: 2.30 [2.12 - 2.62] mmol/L; NPTST064-CMV IGM: NEGATIVE [Not reported - Not reported] Unit not reported; NPTST065-CMV PCR QUANTITATIVE: 32 [Not reported - Not reported] Unit not reported; NPTST132-HEMOGLOBIN A2: 2.6 [1 - 3.5] %; NPTST133-HEMOGLOBIN F: 0.3 [Not reported - 2] %; NPTST165-MAGNESIUM: 0.91 [0.75 - 1.05] mmol/L; NPTST194-PHOSPHATE: 1.45 [0.8 - 1.45] mmol/L; NPTST200-PREALBUMIN: 218 [180 - 380] mg/L; NPTST208-PTT: 33.9 [28.4 - 40.8] sec; NPTST284-VITAMIN D25 TOTAL: 16 [50 - 125] umol/L; Prothrombin Intl. Normalized Ratio: 1.22 [0.9 - 1.1] RATIO; Prothrombin Time: 15.6 [11.9 - 14.7] sec; [redacted]20[redacted] (Rx Day 37): Albumin: 32 [38 - 52] g/L; Calcium: 2.42 [2.12 - 2.62] mmol/L; NPTST165-MAGNESIUM: 0.79 [0.75 - 1.05] mmol/L; NPTST194-PHOSPHATE: 1.27 [0.8 - 1.45] mmol/L; [redacted]20[redacted] (Rx Day 38): Calcium: 2.46 [2.12 - 2.62] mmol/L; NPTST165-MAGNESIUM: 0.89 [0.75 - 1.05] mmol/L; NPTST194-PHOSPHATE: 1.16 [0.8 - 1.45] mmol/L; [redacted]20[redacted] (Rx Day 39): Calcium: 2.26 [2.12 - 2.62] mmol/L; NPTST165-MAGNESIUM: 0.90 [0.75 - 1.05] mmol/L; NPTST194-PHOSPHATE: 1.28 [0.8 - 1.45] mmol/L; [redacted]20[redacted] (Rx Day 40): C Reactive Protein: 6.81 [0 - 5] mg/L; Calcium: 2.31 [2.12 - 2.62] mmol/L; NPTST165-MAGNESIUM: 0.80 [0.75 - 1.05] mmol/L; NPTST194-PHOSPHATE: 1.09 [0.8 - 1.45] mmol/L; [redacted]20[redacted] (Rx Day 41): Calcium: 2.31 [2.12 - 2.62] mmol/L; NPTST165-MAGNESIUM: 0.74 [0.75 - 1.05] mmol/L; NPTST194-PHOSPHATE: 1.04 [0.8 - 1.45] mmol/L; [redacted]20[redacted] (Rx Day 42): Calcium: 2.28 [2.12 - 2.62] mmol/L; NPTST165-MAGNESIUM: 0.80 [0.75 - 1.05] mmol/L; NPTST194-PHOSPHATE: 1.24 [0.8 - 1.45] mmol/L

Microbiology

[redacted]20[redacted] (Rx Day 35): STOOL NPTST053-C-DIFFICILE: NEGATIVE; STOOL NPTST189-PARASITOLOGY DIARRHEA FOR PCR: NEGATIVE-NEGATIVE FOR ALL PARASITES; STOOL NPTST254-STOOL CULTURE: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 23): CT ABDOMEN AND PELVIS: PANCOLITIS AND TERMINAL ILEITIS IN KEEPING WITH CROHN'S DISEASE. THIS CAN REPRESENT AN ACUTE ON CHRONIC INFLAMMATORY PROCESS VS CHRONIC INFLAMMATORY CHANGES, GIVEN NO SIGNIFICANT CHANGE SINCE PRIOR STUDY, FOR CLINICAL CORRELATION. NO ORGANIZED INTRA-

ABDOMINAL OR PELVIC FLUID COLLECTION, ABSCESS OR FISTULA. FOLLOW-UP BY MRI ENTEROGRAPHY IS SUGGESTED.

AE Stopped Rx Day	58
Duration of AE	24 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DISEASE UNDER STUDY. CROHN'S DISEASE EXACERBATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

カナダの治験責任医師からの報告。本被験者は2[redacted]歳男性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，クローン病増悪の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，瘻孔切開，正色素性貧血，クローン病，サイトメガロウイルス（CMV）結腸，クローン病フレア，喫煙者（1 日 15 本を 8 年間）及び非飲酒者であった。

投与 35 日後，被験者はクローン病増悪を発現した。投与 58 日後，クローン病増悪は消失した。

投与 35 日後，被験者は鮮血性下痢（15 回，ベースライン：8 回），非血性嘔吐（4 回）及び 1 週間持続する腹痛悪化のため入院した。腹痛は中心～下腹部にかけてあり，筋痙攣を伴い，中等度～重度の繰り返し発現するものであり，非放散性であり，トラマドールにより部分的に軽減されたと説明された。発熱，悪寒及びメレナは認められなかった。口腔潰瘍，眼病変，関節痛，背部痛及び発疹は認められなかった。最近の旅行歴，食事の変化歴及び病人との接触歴はなかった。

身体的診察時，目の紅斑，結膜炎，口腔潰瘍又は LAD は認められなかった。被験者の両肺に問題はなく，ばち状指は認められなかった。心臓聴診が行われ，s1/2 は正常であった。腹部は膨

張しており，腸雑音亢進もあった。しかし，腹部は軟らかく，弛緩しており，圧痛及び固縮は認められなかった。投与 42 日後，被験者は退院した。

投与された薬剤は，ヒドロモルフォン，ソル・メドロール，Gravol，モルヒネ，カリウム及びオンダンセトロンであった。

The patient’s past medications include:

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

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

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

Causality for RISANKIZUMAB (Blinded)

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

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

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

Dechallenge: Not Applicable

Alternative Etiology for RISANKIZUMAB (Blinded)

Event of CROHN'S DISEASE EXACERBATION

- Investigator: Disease under study. Crohn's Disease exacerbation

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CREATININE:** 85 umol/L (normal 55 to 110)

[redacted] 20[redacted] ALANINE AMINO TRANSFERASE: 12 U/L (normal 6 to 45)

[redacted] **20[redacted] ALBUMIN:** 32 G/L (normal 38 to 52)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 54 U/L (normal 53 to 128)

[redacted] **20[redacted] BILIRUBIN:** 10.0 umol/L (normal 1.7 to 18.9)

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

[redacted] 20[redacted] C-DIFFICILE STOOL TEST: NEGATIVE

[redacted] **20[redacted] CHLORIDE:** 95 MMOL/L (normal 100 to 109)

[redacted] 20[redacted] CMV IGM: Negative

[redacted] 20[redacted] CMV PCR QUANTITATIVE: 32 COPIES/ML

[redacted] **20[redacted] CRP:** 48.43 MG/L (normal 0 to 5.0)

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** Pancolitis and terminal ileitis in keeping with Crohn's Disease. This can represent an acute on chronic inflammatory process vs chronic inflammatory changes, given no significant change since prior study, for clinical correlation. No organized intra-abdominal or pelvic fluid collection, abscess or fistula. Follow-up by MRI enterography is suggested.

[redacted] **20[redacted] HEMATOCRIT:** 0.418 L/L (normal 0.420 to 0.520)

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

[redacted] 20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN: 6.81 MG/L (normal 0.00 to 5.00)

[redacted] **20[redacted] INR:** 1.22 Ratio (normal 0.90 to 1.10)

[redacted] **20[redacted] LIPASE:** 25 U/L (normal 14 to 45)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 3.50 X10**9/L (normal 1.00 to 4.80)

[redacted] **20[redacted] MCV:** 73.7 FL (normal 80 to 100)

[redacted] **20[redacted] NEUTROPHILS ABS:** 10.84 X10**9/L (normal 1.80 to 7.70)

[redacted] 20[redacted] PARASITOLOGY DIARRHEA FOR PCR: Negative for all parasites

[redacted] **20[redacted] PLATELET COUNT:** 457 X10**9/L (normal 140 to 450)

[redacted] **20[redacted] POTASSIUM:** 3.2 MMOL/L (normal 3.5 to 5)

[redacted] **20[redacted] PROTHROMBIN TIME:** 15.6 SEC (normal 11.9 to 14.7)

[redacted] **20[redacted] RED BLOOD CELLS:** 5.67 X10**12/L (normal 4.50 to 5.90)

[redacted] **20[redacted] SODIUM:** 135 MMOL/L (normal 133 to 143)

[redacted] 20[redacted] STOOL CULTURE: NEGATIVE

[redacted] **20[redacted] VITAMIN D25 TOTAL:** 16 umol/L (normal 50 to 125)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 16.00 X10**9/L (normal 4.50 to 11.00)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:RZB 1200 MG IV	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
SEXUALLY TRANSMITTED DISEASE: HERPES	19[redacted]
OTHER: ABDOMINAL PAIN	19
OTHER: BLOATING	19
OTHER: DIARRHEA	19
OTHER: FATIGUE	19
CROHN'S DISEASE	19
OTHER: OSTEOPENIA	20
LIVER DISEASE (EXCLUDING HEPATITIS): FATTY LIVER	20
OTHER: CHRONIC MYOFASCIAL PAIN TO BACK AND SHOULDERS BILATERALLY	20
OTHER: HEADACHES	20
GASTROESOPHAGEAL REFLUX DISEASE	20
OTHER: THORACIC OUTLET SYNDROME	20
OTHER: ALLERGY TO WASPS	20
NEPHROLITHIASIS: KIDNEY STONES	20
OTHER: SHINGLES	20
OTHER: LEFT EAR LABRYNTHITIS	20
ANEMIA: ANEMIA	20
OTHER: BARRETTS ESOPHAGUS	20
OTHER: HEMORRHOIDS	20
OTHER: OVERWEIGHT	20
OTHER: RECTAL BLEEDING	20

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY	20[redacted]
SURGERY: CHOLECYSTECTOMY	20
SURGERY: RT ROTATOR CUFF REPAIR	20
SURGERY: RT ROTATOR CUFF REPAIR	20
SURGERY: LT ROTATOR CUFF REPAIR	20
CROHN'S DISEASE HISTORY: COLONOSCOPY	20

ENDOSCOPY (SCREENING): ILEOCOLONOSCOPY 20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CIGARETTES	FORMER	5 CIGARETTE	7	19[redacted]
CHEWING TOBACCO	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Risankizumab	1200 mg	IV	Every 4 Weeks	[redacted]20[redacted] / 1	[redacted]20[redacted] / 49	49

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day
AZATHIOPRINE	100 mg	QID	Y-M: 20[redacted]
MERCAPTOPURINE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted]
NAPROXEN	2 OTHER: TABS	OTHER: DAILY PRN	Y-M: 20[redacted]
VITAMINS NOS	1 OTHER: TAB	QD	Y-M: 20[redacted]
VITAMINS WITH MINERALS	5000/20 OTHER: IU/MG	QD	Y-M: 20[redacted]
MESALAZINE	4000 mg	QD	Y-M: 20[redacted]
ROBAXISAL COMPUESTO	4-6 OTHER: TABS	OTHER: DAILY PRN	Y-M: 20[redacted]
HYOSCINE	10 mg	OTHER: DAILY PRN	Y-M: 20[redacted]
TRAMADOL	1-2 OTHER: TABS	PRN	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
VITAMINS, OTHER COMBINATIONS	3 OTHER: TABS	QD	Y-M: 20[redacted]
FISH OIL	2000 mg	QD	Y-M: 20[redacted]
MAGNESIUM	1000 mg	QD	Y-M: 20[redacted]
PREDNISONE	50 mg	QD	Y-M: 20[redacted] / -142
IRON	200 mg	OTHER: ONCE	Y-M: 20[redacted] / -31
IRON	200 mg	OTHER: ONCE	Y-M: 20[redacted] / -23
IRON	200 mg	OTHER: ONCE	Y-M: 20[redacted] / -16
IRON	200 mg	OTHER: ONCE	Y-M: 20[redacted] / -10

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Rx Day	Stop Year-Month / Rx Day
NAPROXEN	2 OTHER: TABS	OTHER: DAILY PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
VITAMINS NOS	1 OTHER: TAB	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
VITAMINS WITH MINERALS	5000/20 OTHER: IU/MG	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
ROBAXISAL COMPUESTO	4-6 OTHER: TABS	OTHER: DAILY PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
HYOSCINE	10 mg	OTHER: DAILY PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
TRAMADOL	1-2 OTHER: TABS	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
VITAMINS, OTHER COMBINATIONS	3 OTHER: TABS	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
FISH OIL	2000 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
MAGNESIUM	1000 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 65
DULOXETINE	30 mg	QD	Y-M: 20[redacted] / 22	ONGOING
PREGABALIN	150 mg	QD	Y-M: 20[redacted] / 22	ONGOING
VALACICLOVIR	500 mg	BID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 65
SEMAGLUTIDE	0.25 mg	OTHER: WEEKLY	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 45
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 40
FLUCONAZOLE	150 mg	PRN	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 47
CETIRIZINE	10 mg	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 65
PARACETAMOL	650 mg	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 65
SEMAGLUTIDE	0.5 mg	OTHER: WEEKLY	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 60
LORAZEPAM	2 mg	PRN	Y-M: 20[redacted] / 57	ONGOING
DIMENHYDRINATE	50 mg	OTHER: EVERY 6 HOURS PRN	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 70
MORPHINE	5-10 mg	OTHER: EVERY 2-4 HOURS	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 70

ONDANSETRON	8 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 70
EL-4	UNKNOWN mL	OTHER: CONSTANT INFUSION (ONCE)	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 71
HYOSCINE	10 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 71
HYDROCORTISONE	100 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 73
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 73
DIPHENHYDRAMINE	25 mg	OTHER: ONCE	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 71
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 73	Y-M: 20[redacted] / 80
PREDNISONE	25 mg	OTHER: THIS DOSE WILL TAPER 5 MG WEEKLY TILL COMPLETED TO 0	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 96
CEFAZOLIN	2 g	OTHER: ONCE	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
CLINDAMYCIN	600 mg	PRN	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
FLEBOBAG RING LACT	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
GABAPENTIN	300 mg	OTHER: ONCE	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
GENTAMICIN	240 mg	PRN	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
HEPARIN	5000 IU	OTHER: ONCE	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
METRONIDAZOLE	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
PARACETAMOL	975 mg	OTHER: ONCE	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 98
HYDROCORTISONE	50 mg	OTHER: Q12H	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 99

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

Event Description	SMALL BOWEL OBSTRUCTION
Preferred term	小腸閉塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 69 (20 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

Not reported

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 58): ABDOMINAL SERIES 2 VIEW WITH PA CHEST: CHEST CLEAR. MILD FECAL LOADING NOTED IN THE LARGE BOWEL. FEW SMALL AIR-FLUID LEVELS ARE SEEN IN THE RIGHT LOWER QUADRANT. NO OBVIOUS BOWEL LOOP DILATION NOTED.MULTIPLE METALLIC CLIPS IN THE RIGHTUPPER QUADRANT INDICATE PRIOR CHOLECYSTECTOMY. NO SUSPICIOUS INTRA-ABDOMINAL CALCIFICATIONS OR FREE AIR UNDER THE HEMIDIAPHRAGMS NOTED. REGIONAL OSSEOUS STRUCTURES SHOW NO AGGRESSIVE LESIONS; CT ABDOMEN AND PELVIS AUGMENTED: CHANGES OF TERMINAL ILEITIS WITH STRICTURING INVOLVING A LENGTH OF APPORXIMATELY 6CM. THERE IS RESULTANT SMALL BOWEL OBSTRUCTION SEEN IN THE ILEAL LOOPS AS DESCRIBED ABOVE

AE Stopped Rx Day	73 (24 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	Not reported
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	ILEUM STRICTURE
Preferred term	回腸狭窄
AE Onset Date / Rx Day	[redacted]20[redacted] / 98 (49 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

Not reported

Microbiology

Not reported

SAE Supplemental Procedure

[redacted]20[redacted] (Rx Day 89): CT ABDOMEN AND PELVIS: POST SURGICAL CHANGES OF RECENT LAPROSCOPIC ILEOCOLIC RESCETION. NO ABSTRUCTING RENAL, URETERIC OR BLADDER CALCULUS. THERE IS A N NONOBSTRUCTING 0.4CM LEFT LOWER POLE CALCULU WHICH IS UNCHANGED FROM PRIOR EXAM. NO HYDROURETERONEPHROSIS OR PERINEPHRIC STRANDING. NO SPECIFIC ETIOLOGY FOR THE PATIENTS FLANK PAIN/ VOIDING DYSFUNCTIONS IDENTIFIED.

AE Stopped Rx Day	98 (49 DAYS AFTER LAST TREATMENT)
Duration of AE	1 DAY
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	PREVIOUS SMALL BOWEL OBSTRUCTION.
Discontinued Study Drug Due to the Event	NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-006

カナダの治験責任医師からの報告。本被験者は4[redacted]歳女性であり，AbbVie のリサンキズマブの治験で盲検化された治験薬が投与され，回腸狭窄及び小腸閉塞の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，元喫煙者（1 日 5 本を 7 年間），腹痛，腹部膨満感，下痢，疲労，クローン病，子宮摘出，脂肪肝，胆嚢切除，胃食道逆流性疾患，腎結石，バレット食道，痔核，過体重，直腸出血及び飲酒者（1 日 2 杯未満）であった。

投与 69 日後，被験者は小腸閉塞を発現した。投与 73 日後，小腸閉塞は消失した。投与 98 日後，被験者は回腸狭窄を発現した。投与 98 日後，回腸狭窄は消失した。

投与 69 日後，被験者は悪心，腹痛及び腹部膨満の増加のため入院した。被験者は小腸閉塞と診断され，補液及び IV 薬剤の投与を受けた。投与 73 日後，被験者は退院した。

治験薬の投与は小腸閉塞のため完全に中止された。

投与 98 日後，被験者は小腸閉塞のため再入院し，待機的腹腔鏡下回結腸切除術及び臍ヘルニア修復を受けた。投与 102 日後，被験者は退院した。

投与された薬剤は，生理食塩水，KCL，ブスコパン，ゾフラン，Gravol，モルヒネ，ヒドロコルチゾン，Benadryl，タイレノール，prednisone，硫酸マグネシウム，セファゾリン，ゲンタマイシン，クリンダマイシン，ヘパリン，メトロニダゾール及びガバペンチンであった。

The patient’s past medications include:

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

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

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

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

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

Causality for RISANKIZUMAB (Blinded)

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1) Stricture of ileum (10042236) (Ileal stenosis (10021307)) [v.23.0] [10042236]

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

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

Dechallenge: Not Applicable

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

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 ILEUM STRICTURE

- Investigator: Previous small bowel obstruction.- AbbVie: Event is more likely related to pre-existing crohn's disease.

Event of SMALL BOWEL OBSTRUCTION

- Investigator: Not applicable.

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