表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
皮膚および皮下組織障害 (Cont.)				
寝汗	0	1 (0.3)	0	1 (0.1)
類天疱瘡	0	0	1 (0.7)	1 (0.1)
そう痒症	2 (0.7)	5 (1.6)	0	7 (0.9)
乾癬	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
発疹	6 (2.0)	10 (3.3)	4 (2.6)	20 (2.6)
紅斑性皮疹	0	1 (0.3)	0	1 (0.1)
丘疹性皮疹	0	1 (0.3)	0	1 (0.1)
皮膚病変	2 (0.7)	1 (0.3)	1 (0.7)	4 (0.5)
角層下膿疱性皮膚症	0	1 (0.3)	0	1 (0.1)
蕁麻疹	0	2 (0.7)	0	2 (0.3)
血管障害	1 (0.3)	3 (1.0)	0	4 (0.5)
血腫	0	1 (0.3)	0	1 (0.1)
高血圧	1 (0.3)	2 (0.7)	0	3 (0.4)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent adverse events during the maintenance study are defined as events that begin or worsen either on or after the first dose of the study drug in the maintenance study and within 70 days after the last dose of the study drug.
Event with unknown relationship to study drug is being counted as drug-related.

Cross reference: M14-033 Maintenance Main-study Final CSR_Table 14.3__1.6

M14-033 日本サブ試験 維持療法試験

治験の標題： A Double-Blind, Randomized, Multicenter Study of Higher Versus Standard Adalimumab Dosing Regimens for Induction and Maintenance Therapy in Subjects with Moderately to Severely Active Ulcerative Colitis
施設数 / 実施国名： 主試験：115 施設 / オーストリア，ベルギー，カナダ，チェコ共和国，デンマーク，フランス，ドイツ，ハンガリー，イスラエル，イタリア，オランダ，ポーランド，ルーマニア，スロバキア，スペイン，スイス，ウクライナ，英国及び米国 日本サブ試験：22 施設 / 日本
治験責任医師： [redacted], MD 他
公表文献 (参考資料) ： Panes J, Colombel JF, D'Haens GR, et al. OP216 High versus standard adalimumab induction dosing regimens in patients with moderately to severely active ulcerative colitis: Results from the SERENE UC induction study. United European Gastroenterol J. 2019;7 (Suppl 8S):118. Panes J, Colombel JF, D'Haens GR, et al. OP01 High vs. standard adalimumab maintenance regimens in patients with moderately to severely active ulcerative colitis: Results from the SERENE-UC maintenance study. J Crohns Colitis. 2020;14 (Suppl 1):S001.

治験期間：	開発のフェーズ：
治験開始日（最初の被験者の初回来院日）： 主試験： 2014 年 3 月 27 日（導入療法試験） 20[redacted] 年 [redacted] 月 [redacted] 日（維持療法試験への組入れ時） 日本サブ試験： 2014 年 7 月 22 日（導入療法試験） 20[redacted] 年 [redacted] 月 [redacted] 日（維持療法試験への組入れ時） 治験終了日（最後の被験者の追跡調査終了日）： 主試験： 2019 年 11 月 11 日 日本サブ試験： 20[redacted] 年 [redacted] 月 [redacted] 日	第 III 相

治験の種類： 第 III 相，多施設共同，無作為化，二重盲検試験
目的： 本試験の目的は，中等症から重症の活動性潰瘍性大腸炎（以下「UC」）患者に，高用量での導入療法及び維持療法を行ったときの有効性及び安全性を検討すること，並びに日本人集団と統合集団（日本及び日本以外の治験実施医療機関で登録されたすべての被験者）の間での有効性の一貫性を示すことであった。
被験者数 (計画時と解析時) ： 計画時（導入療法試験） ：940 例（主試験：840 例，日本サブ試験：100 例） 組入れ時（導入療法試験） ：952 例（主試験：852 例，日本サブ試験：100 例） 組入れ時（維持療法試験） ：846 例（主試験：757 例，日本サブ試験：89 例） 解析時（維持療法試験） ：846 例（主試験：757 例，日本サブ試験：89 例）

診断と主要な組入れ基準：

M14-033 試験の主要な選択基準は以下のとおりであった：ベースライン時の年齢が 18 歳以上 75 歳以下の男女。ベースラインの 90 日以上前に UC と診断され，スクリーニング期間中の内視鏡検査（全大腸内視鏡検査又は S 状結腸鏡検査）で診断が確認されると共に，現在の感染症，上皮異形成及び / 又は悪性腫瘍が除外されている患者。治験実施計画書で規定した副腎皮質ステロイドの経口剤又は免疫抑制剤による現在の治療，あるいは医師の判断で十分かつ適切な過去の治療にもかかわらず，ベースラインの Mayo スコア（以下，「FMS」）が 6～12 ポイント，かつ内視鏡所見サブスコアが 2～3 ポイント（中央判定による評価）である活動性の UC 患者。インフリキシマブの投与で以前に UC の治療効果が認められ，その後効果消失又は不耐容となったため，インフリキシマブの投与を中止した患者を，本試験に組み入れることができる（効果消失又は不耐容を示す記録を確認すること）。女性患者の場合は，本試験への参加から 1 年以上前に閉経した，又は不妊手術（両側卵管結紮術，両側卵巣摘出術，及び / 又は子宮摘出術）を行ったことで，妊娠の可能性がないこと。妊娠の可能性がある女性患者の場合は，治験期間中及び治験薬の最終投与日の 150 日後まで，治験実施計画書で規定した方法で避妊すること。女性患者の場合は，治験期間中及び治験薬の最終投与日の 150 日後まで，授乳しないこと。結核スクリーニング検査が陰性の患者。既往歴やスクリーニング期間中に実施する臨床検査，身体的所見，胸部 X 線検査，12 誘導心電図検査の結果から，治験責任医師が健康状態にその他の問題がないと判断した患者。

M14-033 試験の主要な除外基準は以下のとおりであった：クローン病と診断されている，若しくは既往がある，又は indeterminate colitis と診断されている患者。劇症の大腸炎又は中毒性巨大結腸症と診断されている患者。スクリーニング時の内視鏡検査で，病変が直腸のみに限局している患者（潰瘍性直腸炎）。回腸直腸瘻造設を伴う結腸亜全摘術，若しくは回腸嚢，Koch パウチ，回腸ストマ造設を伴う結腸切除術の既往がある患者。又は腸管の手術を予定している患者。

治験方法：

M14-033 試験は，導入療法試験と維持療法試験で構成される。また，日本以外の他国の治験実施医療機関で登録された被験者を対象とした主試験と，日本の治験実施医療機関で登録された被験者を対象とした日本サブ試験で構成される。M14-033 試験では，高用量の導入療法及び維持療法を，承認されている標準用量の導入療法及び維持療法と比較した。また，統合集団でのみ，薬物治療モニタリング（以下「TDM」）戦略を用いた探索的な維持療法も実施した。すべての選択基準を満たし，いずれの除外基準にも抵触しない中等症から重症の成人活動性 UC 患者を本試験の参加に適格とした。

本報告では，日本及び日本以外の治験実施医療機関で登録されたすべての被験者（統合集団）並びに日本の治験実施医療機関で登録されたすべての被験者（日本人集団）を対象とした，M14-033 維持療法試験の解析結果を示す。本報告には，最後の被験者の最終投与 70 日後の追跡調査までに得られたデータを含める（追跡調査終了日：2019 年 11 月 11 日）。本報告は，維持療法試験（主試験及び日本サブ試験）の組織学検査データ，及び前版からの最終的なデータの変更を反映した治験総括報告書の最終版（データベースロック日：20[redacted] 年 [redacted] 月 [redacted] 日）に基づいている。

被験薬，用量，投与方法及びバッチ番号：

投与 8 週時に，日本以外の治験実施施設で登録された被験者を 40 mg 週 1 回投与群，40 mg 隔週投与群又は TDM 群のいずれかに 2：2：1 の比率で再無作為化した。また，日本の治験実施施設で登録された被験者を 40 mg 週 1 回投与群又は 40 mg 隔週投与群のいずれかに 1：1 の比率で再無作為化した。投与 8 週時の再無作為化では，導入療法試験での治療，及び投与 8 週時における改善の有無（治験実施医療機関から提供された投与 8 週時の内視鏡サブスコアを用いた FMS に基づく）を因子として被験者を再度層別化した。投与 8 週時の改善例では，再割付け時に，投与 8 週時の寛解の有無（治験実施医療機関から提供された投与 8 週時の内視鏡サブスコアを用いた FMS に基づく）で更に層別化した。

40 mg 隔週投与群の被験者は，本試験の終了までアダリムマブ 40 mg の隔週投与を継続した。40 mg 週 1 回投与群の被験者は，投与 8 週時にアダリムマブ 40 mg の週 1 回投与を開始し，本試験の終了まで継続した。

TDM 群の被験者は，投与 8 及び 10 週時にアダリムマブ 40 mg の隔週投与を受けた。また，投与 12，24 及び 37 週時に，直前の来院時（それぞれ投与 10，22 及び 35 週時）に盲検下でアダリムマブの血清中濃度を評価した結果，並びに直前及び当該来院時の直腸出血サブスコアに基づき，アダリムマブの用量を調整できることとした。

ロット番号：

アダリムマブ：[redacted]，[redacted]，[redacted]，[redacted]，[redacted]，[redacted]，[redacted]（主試験）
[redacted]，[redacted]，[redacted]（日本サブ試験）

プラセボ：[redacted]，[redacted]，[redacted]，[redacted]，[redacted]（主試験）
[redacted]，[redacted]（日本サブ試験）

治療期間：44 週間

対照薬，用量，投与方法及びバッチ番号：

なし

評価基準：

有効性：

維持療法試験の主要評価項目は，投与 8 週時に FMS で改善例（ベースラインからの FMS の減少が 3 以上かつ 30%以上，更に直腸出血サブスコアの減少が 1 以上あるいは直腸出血サブスコアが 0 又は 1）となり，かつ投与 52 週時に FMS で寛解（FMS が 2 以下で，かついずれのサブスコアも 1 を超えない）を達成した被験者の割合であった。

維持療法試験における順位付き副次評価項目（昇順に順位を階層化）は以下のとおりであった。

1. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に内視鏡検査で改善（内視鏡所見サブスコアが 0 又は 1）が認められた被験者の割合
2. ベースラインで副腎皮質ステロイドを投与しており，投与 8 週時に FMS で改善例となり，かつ投与 52 週時に副腎皮質ステロイドを 90 日間以上離脱できた被験者の割合
3. ベースラインで副腎皮質ステロイドを投与しており，投与 8 週時に FMS で改善例となり，かつ投与 52 週時に副腎皮質ステロイドを 90 日間以上離脱でき，更に FMS で寛解を達成した被験者の割合
4. 投与 8 週時，投与 52 週時にいずれも FMS で寛解例となった被験者の割合
5. 投与 8 週時に FMS で寛解例となり，かつ投与 52 週時に内視鏡検査で改善（内視鏡所見サブスコアが 0 又は 1）が認められた被験者の割合
6. ベースラインで副腎皮質ステロイドを投与していた被験者で，投与 8 週時に FMS で寛解例となり，かつ投与 52 週時に副腎皮質ステロイドを 90 日間以上離脱できた被験者の割合
7. ベースラインで副腎皮質ステロイドを投与していた被験者で，投与 8 週時に FMS で寛解例となり，かつ

投与 52 週時に副腎皮質ステロイドを 90 日間以上離脱でき，更に FMS で寛解を達成した被験者の割合

8. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に Inflammatory Bowel Disease Questionnaire（以下「IBDQ」）で改善（ベースラインと比較して IBDQ スコアの 16 以上の増加）が認められた被験者の割合
9. 投与 8 週時に FMS で非改善例であった被験者のうち，投与 52 週時に FMS で寛解を達成した被験者の割合
10. 投与 8 週時に FMS で非寛解例であった被験者のうち，投与 52 週時に FMS で寛解を達成した被験者の割合
11. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に内視鏡所見サブスコアが 0 ポイントになった被験者の割合
12. 投与 8 週時に FMS で寛解例となり，かつ投与 52 週時に内視鏡所見サブスコアが 0 ポイントになった被験者の割合
13. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に IBDQ の腸症状ドメインで改善（ベースラインと比較して IBDQ の腸症状ドメインのスコアの 6 以上の増加）が認められた被験者の割合
14. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に IBDQ の疲労に関する項目で改善（ベースラインと比較して IBDQ の疲労に関する項目のスコアの 1 以上の増加）が認められた被験者の割合

薬物動態：
別途報告書に記載することとした。
安全性：
治験期間中の有害事象，バイタルサインの変化，身体的所見，及び臨床検査値を評価した。

統計手法：
有効性：
日本サブ試験の維持療法試験では，統合 Intent-to-treat（以下「ITT」）集団及び日本人 ITT 集団を対象に，アダリムマブ 40 mg の週 1 回投与とアダリムマブ 40 mg の隔週投与を比較した。欠測値の補完には，欠測値を「非反応」としてデータ補完する統計手法を用いた（以下「NRI」）。カテゴリカル変数である投与 52 週時の副次評価項目については，導入療法試験での治療，及び投与 8 週時における改善 / 寛解の有無で調整した両側 Cochran-Mantel-Haenszel（以下「CMH」）検定を用いて解析した。また，CMH 検定に基づき，割合の群間差の両側 95%信頼区間を算出した。主要評価項目の感度分析として，治療群，層別化割付け因子及びベースライン時点における免疫抑制剤の使用，ベースライン時の高感度 CRP 値，ベースライン時の重症度などの臨床的に重要な因子を用いた Logistic 回帰分析を実施した。
薬物動態：
別途報告書に記載することとした。
安全性：
日本サブ試験の維持療法試験では，安全性の解析はすべて統合安全性解析対象集団及び日本人安全性解析対象集団を対象に実施した。被験者が実際に受けた治療に基づき，治療群ごとに安全性評価項目を要約した。安全性評価項目の 40 mg 週 1 回投与群と 40 mg 隔週投与群の群間差は，有意水準 0.05 の両側検定を用いて評価した。
特に断らない限り，連続変数の安全性評価項目（例：臨床検査値のベースラインから最終測定時までの変化量）の群間差は，治療を因子とした分散分析モデルを用いて評価した。また，カテゴリカル変数の安全性評価項目の群間差は，Fisher の正確確率検定を用いて評価した。

要約 / 結論：

有効性：

統合 ITT 集団では，投与 8 週時に FMS で改善例となり，かつ投与 52 週時に FMS で寛解を達成した被験者の割合は，40 mg 週 1 回投与群の方が 40 mg 隔週投与群よりも統計学的に有意に高かった。部分集団解析の結果は，主解析の結果とおおむね一致していた。

日本人 ITT 集団では，投与 8 週時に FMS で改善例となり，かつ投与 52 週時に FMS で寛解を達成した被験者の割合は，40 mg 週 1 回投与群の方が 40 mg 隔週投与群よりも数値的に高かった。部分集団解析の結果は，ベースラインにおける FMS（9 以下 / 9 超），ベースラインにおける FMS（中央値以下 / 中央値超），ベースラインにおける全大腸炎の有無，ベースラインにおける高感度 C 反応性たん白（以下「hs-CRP」）（5 mg/L 以下 / 5 mg/L 超）及びベースラインにおける hs-CRP（中央値以下 / 中央値超）を除き，主解析の結果とおおむね一致していた。

統合 ITT 集団では，各順位付き副次評価項目を達成した被験者の割合は，40 mg 週 1 回投与群の方が 40 mg 隔週投与群よりも数値的に高かった。

日本人 ITT 集団では，順位付き副次評価項目のうち 8 項目について，達成した被験者の割合が 40 mg 週 1 回投与群の方が 40 mg 隔週投与群よりも数値的に高かった。

薬物動態：

別途報告書に記載することとした。

安全性：

統合安全性解析対象集団及び日本人安全性解析対象集団のいずれにおいても，アダリムマブの安全性プロファイルは，40 mg 週 1 回投与群，40 mg 隔週投与群及び TDM 群（統合集団のみ）で同様であり，アダリムマブの既知の安全性プロファイルと一致していた。新たな安全性シグナル又は予期しない傾向は認められなかった。

統合安全性解析対象集団及び日本人安全性解析対象集団のいずれにおいても，各投与群の被験者の大部分に 1 件以上の有害事象が発現した。維持療法試験中，4 例が死亡した。いずれも主試験の被験者であり，2 例は 40 mg 週 1 回投与群の被験者，2 例は 40 mg 隔週投与群の被験者であった。いずれの死亡も治験薬との因果関係は関連なしと判断された。いずれの集団においても，有害事象及び重篤な有害事象の発現割合は投与群間で同程度であった。統合安全性解析対象集団では，重篤な有害事象が 103 例（12.2%）に発現し，治験薬投与の中止に至った有害事象が 92 例（10.9%）に発現した。日本人安全性解析対象集団では，重篤な有害事象が 6 例（6.7%）に発現し，治験薬投与の中止に至った有害事象が 7 例（7.9%）に発現した。

統合安全性解析対象集団で最も多く報告された器官別大分類（以下「SOC」）は，いずれの投与群でも胃腸障害（40 mg 週 1 回投与群：33.1%，40 mg 隔週投与群：40.0%，TDM 群：29.8%）及び感染症および寄生虫症（40 mg 週 1 回投与群：38.3%，40 mg 隔週投与群：40.0%，TDM 群：34.4%）であった。最も多く（被験者の 5%以上）報告された基本語（以下「PT」）は，潰瘍性大腸炎，上咽頭炎，関節痛，上気道感染及び頭痛であった。

日本人安全性解析対象集団で最も多く報告された SOC は，いずれの投与群でも感染症および寄生虫症（40 mg 週 1 回投与群：60.9%，40 mg 隔週投与群：55.8%），胃腸障害（40 mg 週 1 回投与群：28.3%，40 mg 隔週投与群：23.3%）及び皮膚および皮下組織障害（40 mg 週 1 回投与群：21.7%，40 mg 隔週投与群：14.0%）であった。最も多く（被験者の 5%以上）報告された PT は，上咽頭炎，貧血，インフルエンザ，潰瘍性大腸炎，発熱，悪心及び膀胱炎であった。

統合安全性解析対象集団及び日本人安全性解析対象集団のいずれにおいても，特に注目すべき有害事象（以下「AESI」）の発現割合は，感染症及び血液障害を除き，全般的に低かった（5%未満）。いずれの AESI も発現割合は投与群間でおおむね同程度であった。

臨床検査（血液学的検査，血液生化学検査及び尿検査）の平均値にベースラインからの顕著な変化は認められなかった。血液学的検査，血液生化学検査値及び尿検査値に関して，ベースラインが正常値若しくは異常高値であった検査値が最終測定時に異常低値に変動した被験者，及びベースラインが異常低値若しくは正常値であった検査値が最終測定時に異常高値に変動した被験者は少数であり，臨床的に重要ではないと判断された。

バイタルサインの平均値にベースラインからの顕著な変化は認められなかった。

維持療法試験中，5 例の妊娠が報告された。いずれも主試験の被験者であり，妊娠の転帰は，先天性異常なしの出産が 4 例，妊娠前期での自然流産が 1 例であった。

治験期間中，予期しない治験薬又は機器の問題は認められなかった。

結論：

統合集団では，投与 8 週時に FMS で改善例となり，かつ投与 52 週時に FMS で寛解を達成した被験者の割合は，40 mg 週 1 回投与群の方が 40 mg 隔週投与群よりも統計学的に有意に高かった。

日本人集団では，投与 8 週時に FMS で改善例となり，かつ投与 52 週時に FMS で寛解を達成した被験者の割合は，40 mg 週 1 回投与群の方が 40 mg 隔週投与群よりも数値的に高かった。

アダリムマブ維持療法の安全性プロファイルは，統合集団及び日本人集団で同様であり，アダリムマブの既知の安全性プロファイルと一致していた。新たな安全性のシグナル又は予期しない傾向は認められなかった。全体として，本試験の対象集団における標準用量のアダリムマブ維持療法のベネフィット・リスクプロファイルは不変であった。

表 1. すべての有害事象（MedDRA SOC 及び PT 別）
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MedDRA 22.0 System Organ Class Preferred Term	Japan Safety Set Adalimumab 40mg EOW (N=43) n (%)	Japan Safety Set Adalimumab 40mg EW (N=46) n (%)	Japan Safety Set Adalimumab Total (N=89) n (%)	Integrated Safety Set Adalimumab 40mg EOW (N=345) n (%)	Integrated Safety Set Adalimumab 40mg EW (N=350) n (%)	Integrated Safety Set Adalimumab TDM Regimen (N=151) n (%)	Integrated Safety Set Adalimumab Total (N=846) n (%)
Any Adverse Event	37 (86.0)	41 (89.1)	78 (87.6)	257 (74.5)	263 (75.1)	96 (63.6)	616 (72.8)
血液およびリンパ系障害	4 (9.3)	6 (13.0)	10 (11.2)	21 (6.1)	32 (9.1)	9 (6.0)	62 (7.3)
貧血	3 (7.0)	5 (10.9)	8 (9.0)	15 (4.3)	18 (5.1)	5 (3.3)	38 (4.5)
内出血発生の増加傾向	0	0	0	0	1 (0.3)	0	1 (0.1)
鉄欠乏性貧血	1 (2.3)	0	1 (1.1)	3 (0.9)	2 (0.6)	0	5 (0.6)
白血球増加症	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
白血球減少症	0	1 (2.2)	1 (1.1)	1 (0.3)	5 (1.4)	0	6 (0.7)
リンパ節症	0	0	0	0	2 (0.6)	1 (0.7)	3 (0.4)
リンパ球減少症	0	0	0	0	0	1 (0.7)	1 (0.1)
好中球減少症	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
血小板減少症	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
血小板増加症	0	0	0	1 (0.3)	3 (0.9)	0	4 (0.5)
心臓障害	0	0	0	6 (1.7)	4 (1.1)	1 (0.7)	11 (1.3)
急性心筋梗塞	0	0	0	1 (0.3)	0	0	1 (0.1)
心房細動	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
うっ血性心不全	0	0	0	1 (0.3)	0	0	1 (0.1)
冠動脈疾患	0	0	0	1 (0.3)	0	0	1 (0.1)

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心臓障害 (Cont.)							
心筋虚血	0	0	0	1 (0.3)	0	0	1 (0.1)
動悸	0	0	0	2 (0.6)	2 (0.6)	0	4 (0.5)
洞性徐脈	0	0	0	0	1 (0.3)	0	1 (0.1)
頻脈	0	0	0	1 (0.3)	0	0	1 (0.1)
耳および迷路障害	2 (4.7)	0	2 (2.2)	7 (2.0)	3 (0.9)	1 (0.7)	11 (1.3)
感音性難聴	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
外耳道狭窄	0	0	0	1 (0.3)	0	0	1 (0.1)
耳痛	0	0	0	0	1 (0.3)	0	1 (0.1)
耳鳴	0	0	0	2 (0.6)	2 (0.6)	1 (0.7)	5 (0.6)
回転性めまい	1 (2.3)	0	1 (1.1)	3 (0.9)	0	0	3 (0.4)
内分泌障害	0	0	0	3 (0.9)	3 (0.9)	0	6 (0.7)
クッシング様症状	0	0	0	2 (0.6)	0	0	2 (0.2)
甲状腺腫	0	0	0	0	1 (0.3)	0	1 (0.1)
甲状腺機能低下症	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
眼障害	2 (4.7)	1 (2.2)	3 (3.4)	11 (3.2)	17 (4.9)	2 (1.3)	30 (3.5)
閉塞隅角緑内障	0	0	0	0	1 (0.3)	0	1 (0.1)
乱視	0	0	0	0	1 (0.3)	0	1 (0.1)

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眼障害 (Cont.)							
眼瞼炎	0	0	0	0	1 (0.3)	0	1 (0.1)
眼瞼痙攣	0	0	0	0	2 (0.6)	0	2 (0.2)
白内障	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
アレルギー性結膜炎	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
複視	0	0	0	0	1 (0.3)	0	1 (0.1)
ドライアイ	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
上強膜炎	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
眼瞼紅斑	0	0	0	1 (0.3)	0	0	1 (0.1)
眼の炎症	0	0	0	0	1 (0.3)	0	1 (0.1)
眼刺激	0	0	0	0	1 (0.3)	0	1 (0.1)
眼痛	0	0	0	1 (0.3)	0	0	1 (0.1)
眼瞼縁痂皮	0	0	0	0	1 (0.3)	0	1 (0.1)
眼瞼下垂	0	0	0	0	2 (0.6)	0	2 (0.2)
眼瞼そう痒症	0	0	0	1 (0.3)	0	0	1 (0.1)
緑内障	0	1 (2.2)	1 (1.1)	1 (0.3)	1 (0.3)	0	2 (0.2)
眼充血	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
眼酒さ	0	0	0	0	1 (0.3)	0	1 (0.1)

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眼障害 (Cont.)							
視神経萎縮	0	0	0	1 (0.3)	0	0	1 (0.1)
老視	0	0	0	0	1 (0.3)	0	1 (0.1)
網膜剥離	0	0	0	1 (0.3)	0	0	1 (0.1)
眼瞼腫脹	0	0	0	0	3 (0.9)	0	3 (0.4)
霧視	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
視力低下	0	0	0	1 (0.3)	0	0	1 (0.1)
視力障害	0	0	0	1 (0.3)	0	0	1 (0.1)
胃腸障害	10 (23.3)	13 (28.3)	23 (25.8)	138 (40.0)	116 (33.1)	45 (29.8)	299 (35.3)
腹部不快感	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
腹部膨満	0	1 (2.2)	1 (1.1)	5 (1.4)	2 (0.6)	1 (0.7)	8 (0.9)
腹部ヘルニア	0	0	0	1 (0.3)	0	0	1 (0.1)
腹痛	1 (2.3)	0	1 (1.1)	8 (2.3)	6 (1.7)	1 (0.7)	15 (1.8)
下腹部痛	0	0	0	2 (0.6)	2 (0.6)	0	4 (0.5)
上腹部痛	0	1 (2.2)	1 (1.1)	3 (0.9)	7 (2.0)	1 (0.7)	11 (1.3)
腹部圧痛	0	0	0	2 (0.6)	0	1 (0.7)	3 (0.4)
後天性食道ウエッブ	0	0	0	0	1 (0.3)	0	1 (0.1)
裂肛	0	1 (2.2)	1 (1.1)	0	5 (1.4)	0	5 (0.6)

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胃腸障害 (Cont.)							
肛門出血	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
肛門失禁	0	0	0	0	1 (0.3)	0	1 (0.1)
肛門そう痒症	0	0	0	0	0	1 (0.7)	1 (0.1)
肛門性器異形成	0	0	0	0	2 (0.6)	0	2 (0.2)
アフタ性潰瘍	1 (2.3)	0	1 (1.1)	1 (0.3)	0	1 (0.7)	2 (0.2)
呼気臭	0	0	0	1 (0.3)	0	0	1 (0.1)
口唇のひび割れ	0	0	0	1 (0.3)	0	0	1 (0.1)
口唇炎	0	0	0	0	0	1 (0.7)	1 (0.1)
大腸炎	0	0	0	6 (1.7)	1 (0.3)	1 (0.7)	8 (0.9)
潰瘍性大腸炎	2 (4.7)	5 (10.9)	7 (7.9)	76 (22.0)	65 (18.6)	29 (19.2)	170 (20.1)
結腸異形成	0	0	0	1 (0.3)	0	0	1 (0.1)
便秘	0	0	0	3 (0.9)	5 (1.4)	1 (0.7)	9 (1.1)
クローン病	0	0	0	0	1 (0.3)	0	1 (0.1)
便意切迫	0	0	0	0	1 (0.3)	0	1 (0.1)
齲歯	1 (2.3)	1 (2.2)	2 (2.2)	3 (0.9)	2 (0.6)	0	5 (0.6)
歯嚢胞	1 (2.3)	0	1 (1.1)	2 (0.6)	0	0	2 (0.2)
下痢	1 (2.3)	0	1 (1.1)	11 (3.2)	7 (2.0)	1 (0.7)	19 (2.2)

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胃腸障害 (Cont.)							
憩室	0	0	0	0	2 (0.6)	0	2 (0.2)
口内乾燥	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
穿孔性十二指腸潰瘍	0	0	0	0	1 (0.3)	0	1 (0.1)
十二指腸炎	0	0	0	0	1 (0.3)	0	1 (0.1)
十二指腸胃逆流	0	0	0	0	0	1 (0.7)	1 (0.1)
排便困難	0	0	0	0	1 (0.3)	0	1 (0.1)
消化不良	1 (2.3)	0	1 (1.1)	4 (1.2)	4 (1.1)	3 (2.0)	11 (1.3)
嚥下障害	0	1 (2.2)	1 (1.1)	0	4 (1.1)	0	4 (0.5)
小腸炎	0	0	0	0	1 (0.3)	0	1 (0.1)
鼓腸	0	0	0	3 (0.9)	1 (0.3)	4 (2.6)	8 (0.9)
排便回数増加	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
胃炎	0	1 (2.2)	1 (1.1)	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
びらん性胃炎	0	0	0	0	2 (0.6)	1 (0.7)	3 (0.4)
胃腸障害	1 (2.3)	0	1 (1.1)	2 (0.6)	0	0	2 (0.2)
胃腸の炎症	0	0	0	1 (0.3)	0	0	1 (0.1)
胃食道逆流性疾患	0	0	0	0	7 (2.0)	1 (0.7)	8 (0.9)
歯肉出血	0	0	0	0	1 (0.3)	0	1 (0.1)

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胃腸障害 (Cont.)							
歯肉障害	0	0	0	1 (0.3)	0	0	1 (0.1)
舌炎	0	1 (2.2)	1 (1.1)	1 (0.3)	1 (0.3)	0	2 (0.2)
血便排泄	0	0	0	1 (0.3)	0	0	1 (0.1)
痔出血	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
痔核	1 (2.3)	2 (4.3)	3 (3.4)	8 (2.3)	8 (2.3)	1 (0.7)	17 (2.0)
裂孔ヘルニア	0	0	0	0	1 (0.3)	0	1 (0.1)
過敏性腸症候群	0	2 (4.3)	2 (2.2)	0	2 (0.6)	0	2 (0.2)
大腸ポリープ	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
マロリー・ワイス症候群	0	0	0	0	0	1 (0.7)	1 (0.1)
口腔内潰瘍形成	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
粘液便	0	0	0	1 (0.3)	0	0	1 (0.1)
悪心	1 (2.3)	4 (8.7)	5 (5.6)	14 (4.1)	10 (2.9)	3 (2.0)	27 (3.2)
口腔障害	0	0	0	0	0	1 (0.7)	1 (0.1)
膵不全	0	0	0	1 (0.3)	0	0	1 (0.1)
急性膵炎	0	0	0	1 (0.3)	0	0	1 (0.1)
肛門周囲痛	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
直腸炎	0	0	0	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）
（統合安全性解析対象集団及び日本人安全性解析対象集団，M14-033 日本サブ試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Japan Safety Set Adalimumab 40mg EOW (N=43) n (%)	Japan Safety Set Adalimumab 40mg EW (N=46) n (%)	Japan Safety Set Total (N=89) n (%)	Integrated Safety Set Adalimumab 40mg EOW (N=345) n (%)	Integrated Safety Set Adalimumab 40mg EW (N=350) n (%)	Integrated Safety Set TDM Regimen (N=151) n (%)	Integrated Safety Set Total (N=846) n (%)
胃腸障害 (Cont.)							
偽性ポリポーシス	0	0	0	1 (0.3)	0	0	1 (0.1)
直腸出血	0	0	0	2 (0.6)	4 (1.1)	0	6 (0.7)
直腸ポリープ	0	0	0	1 (0.3)	0	0	1 (0.1)
唾液腺障害	0	0	0	0	1 (0.3)	0	1 (0.1)
小腸閉塞	0	0	0	0	0	1 (0.7)	1 (0.1)
口内炎	0	0	0	1 (0.3)	0	0	1 (0.1)
歯の障害	0	0	0	0	2 (0.6)	1 (0.7)	3 (0.4)
埋伏歯	0	0	0	1 (0.3)	0	0	1 (0.1)
歯痛	0	0	0	4 (1.2)	6 (1.7)	1 (0.7)	11 (1.3)
上部消化管出血	0	0	0	0	0	1 (0.7)	1 (0.1)
嘔吐	0	1 (2.2)	1 (1.1)	7 (2.0)	9 (2.6)	2 (1.3)	18 (2.1)
一般・全身障害および投与部位の状態	4 (9.3)	6 (13.0)	10 (11.2)	44 (12.8)	57 (16.3)	12 (7.9)	113 (13.4)
医薬品副作用	0	0	0	0	1 (0.3)	0	1 (0.1)
無力症	0	0	0	4 (1.2)	7 (2.0)	2 (1.3)	13 (1.5)
胸部不快感	0	0	0	0	1 (0.3)	0	1 (0.1)
胸痛	0	0	0	6 (1.7)	2 (0.6)	0	8 (0.9)
悪寒	0	0	0	2 (0.6)	1 (0.3)	0	3 (0.4)

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一般・全身障害および投与部位の状態 (Cont.)							
嚢胞	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
不快感	0	0	0	1 (0.3)	0	0	1 (0.1)
薬物相互作用	0	0	0	0	1 (0.3)	0	1 (0.1)
異形成	0	0	0	1 (0.3)	0	2 (1.3)	3 (0.4)
早期満腹	0	0	0	1 (0.3)	0	0	1 (0.1)
疲労	0	0	0	4 (1.2)	6 (1.7)	0	10 (1.2)
歩行障害	0	0	0	1 (0.3)	0	0	1 (0.1)
異常高熱	0	0	0	0	1 (0.3)	0	1 (0.1)
高熱	0	0	0	0	0	1 (0.7)	1 (0.1)
インフルエンザ様疾患	0	0	0	2 (0.6)	4 (1.1)	0	6 (0.7)
注入部位紅斑	0	0	0	0	1 (0.3)	0	1 (0.1)
注入部位血腫	0	0	0	0	0	1 (0.7)	1 (0.1)
注入部位そう痒感	0	0	0	0	1 (0.3)	0	1 (0.1)
注射部位紅斑	0	0	0	3 (0.9)	2 (0.6)	1 (0.7)	6 (0.7)
注射部位過敏反応	0	0	0	0	1 (0.3)	0	1 (0.1)
注射部位硬結	0	0	0	1 (0.3)	0	0	1 (0.1)
注射部位炎症	0	0	0	0	2 (0.6)	0	2 (0.2)

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一般・全身障害および投与部位の状態 (Cont.)							
注射部位結節	0	0	0	1 (0.3)	0	0	1 (0.1)
注射部位疼痛	0	0	0	2 (0.6)	2 (0.6)	0	4 (0.5)
注射部位そう痒感	0	0	0	0	2 (0.6)	1 (0.7)	3 (0.4)
注射部位発疹	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
注射部位反応	0	1 (2.2)	1 (1.1)	2 (0.6)	3 (0.9)	3 (2.0)	8 (0.9)
注射部位腫脹	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
限局性浮腫	0	0	0	1 (0.3)	0	0	1 (0.1)
倦怠感	1 (2.3)	1 (2.2)	2 (2.2)	1 (0.3)	1 (0.3)	0	2 (0.2)
小結節	0	0	0	0	1 (0.3)	0	1 (0.1)
非心臓性胸痛	0	0	0	1 (0.3)	0	0	1 (0.1)
浮腫	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
末梢性浮腫	0	0	0	4 (1.2)	2 (0.6)	0	6 (0.7)
疼痛	0	0	0	2 (0.6)	4 (1.1)	0	6 (0.7)
末梢腫脹	0	0	0	2 (0.6)	1 (0.3)	0	3 (0.4)
ポリープ	0	0	0	0	0	1 (0.7)	1 (0.1)
偽ポリープ	0	0	0	0	1 (0.3)	0	1 (0.1)
発熱	2 (4.7)	4 (8.7)	6 (6.7)	10 (2.9)	16 (4.6)	1 (0.7)	27 (3.2)

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一般・全身障害および投与部位の状態 (Cont.)							
腫脹	0	0	0	1 (0.3)	3 (0.9)	0	4 (0.5)
圧痛	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
組織変色	0	0	0	0	0	1 (0.7)	1 (0.1)
血管穿刺部位血腫	0	0	0	0	1 (0.3)	0	1 (0.1)
肝胆道系障害	1 (2.3)	2 (4.3)	3 (3.4)	4 (1.2)	6 (1.7)	7 (4.6)	17 (2.0)
胆管結石	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
胆石症	0	0	0	1 (0.3)	0	0	1 (0.1)
胆嚢ポリープ	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
肝機能異常	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
脂肪肝	0	0	0	0	1 (0.3)	0	1 (0.1)
肝胆道系疾患	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
高ビリルビン血症	0	0	0	0	1 (0.3)	0	1 (0.1)
高トランスアミナーゼ血症	0	0	0	1 (0.3)	1 (0.3)	4 (2.6)	6 (0.7)
肝損傷	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
非アルコール性脂肪性肝炎	0	0	0	1 (0.3)	0	0	1 (0.1)
門脈脾静脈腸間膜静脈血栓症	0	0	0	0	0	1 (0.7)	1 (0.1)

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免疫系障害	0	2 (4.3)	2 (2.2)	2 (0.6)	6 (1.7)	1 (0.7)	9 (1.1)
節足動物刺傷アレルギー	0	0	0	0	1 (0.3)	0	1 (0.1)
薬物過敏症	0	0	0	1 (0.3)	0	0	1 (0.1)
過敏症	0	0	0	0	1 (0.3)	0	1 (0.1)
複合アレルギー	0	0	0	0	1 (0.3)	0	1 (0.1)
季節性アレルギー	0	2 (4.3)	2 (2.2)	1 (0.3)	3 (0.9)	1 (0.7)	5 (0.6)
感染症および寄生虫症	24 (55.8)	28 (60.9)	52 (58.4)	138 (40.0)	134 (38.3)	52 (34.4)	324 (38.3)
四肢膿瘍	0	0	0	0	2 (0.6)	0	2 (0.2)
急性副鼻腔炎	0	0	0	0	2 (0.6)	0	2 (0.2)
肛門膿瘍	0	0	0	0	1 (0.3)	0	1 (0.1)
虫垂炎	0	0	0	0	1 (0.3)	0	1 (0.1)
無症候性細菌尿	0	0	0	0	1 (0.3)	0	1 (0.1)
細菌感染	0	1 (2.2)	1 (1.1)	1 (0.3)	1 (0.3)	0	2 (0.2)
細菌性腟症	0	0	0	0	1 (0.3)	0	1 (0.1)
細菌性外陰腟炎	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
気管支炎	1 (2.3)	1 (2.2)	2 (2.2)	5 (1.4)	2 (0.6)	3 (2.0)	10 (1.2)
カンジダ感染	0	0	0	1 (0.3)	2 (0.6)	1 (0.7)	4 (0.5)
蜂巣炎	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)

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感染症および寄生虫症 (Cont.)							
クロストリジウム・ディフィシレ感染	0	0	0	4 (1.2)	2 (0.6)	0	6 (0.7)
結膜炎	0	0	0	5 (1.4)	2 (0.6)	3 (2.0)	10 (1.2)
膀胱炎	2 (4.7)	3 (6.5)	5 (5.6)	3 (0.9)	3 (0.9)	2 (1.3)	8 (0.9)
サイトメガロウイルス感染	0	0	0	1 (0.3)	0	0	1 (0.1)
憩室炎	0	0	0	0	1 (0.3)	0	1 (0.1)
耳感染	0	0	0	3 (0.9)	2 (0.6)	3 (2.0)	8 (0.9)
蟯虫症	0	0	0	0	2 (0.6)	0	2 (0.2)
エプスタイン・バーウイルス感染	0	0	0	2 (0.6)	0	0	2 (0.2)
外耳蜂巣炎	0	0	0	1 (0.3)	0	0	1 (0.1)
眼瞼感染	0	0	0	0	1 (0.3)	0	1 (0.1)
毛包炎	0	0	0	0	4 (1.1)	1 (0.7)	5 (0.6)
真菌感染	0	0	0	1 (0.3)	0	0	1 (0.1)
皮膚真菌感染	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
せつ	0	0	0	1 (0.3)	0	0	1 (0.1)
胃腸炎	1 (2.3)	0	1 (1.1)	6 (1.7)	5 (1.4)	2 (1.3)	13 (1.5)
細菌性胃腸炎	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
ウイルス性胃腸炎	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)

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感染症および寄生虫症 (Cont.)							
消化管感染	0	0	0	1 (0.3)	0	0	1 (0.1)
性器カンジダ症	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
歯肉膿瘍	0	0	0	0	1 (0.3)	0	1 (0.1)
ヘリコバクター感染	0	0	0	1 (0.3)	0	0	1 (0.1)
ヘルペス眼感染	0	0	0	0	1 (0.3)	0	1 (0.1)
単純ヘルペス	0	0	0	2 (0.6)	0	0	2 (0.2)
帯状疱疹	0	0	0	3 (0.9)	3 (0.9)	1 (0.7)	7 (0.8)
麦粒腫	0	1 (2.2)	1 (1.1)	1 (0.3)	3 (0.9)	0	4 (0.5)
膿痂疹	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
インフルエンザ	3 (7.0)	4 (8.7)	7 (7.9)	16 (4.6)	15 (4.3)	5 (3.3)	36 (4.3)
喉頭炎	0	0	0	1 (0.3)	0	0	1 (0.1)
限局性感染	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
下気道感染	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
ライム病	0	0	0	1 (0.3)	0	0	1 (0.1)
伝染性軟属腫	0	0	0	0	1 (0.3)	0	1 (0.1)
鼓膜炎	0	0	0	0	0	1 (0.7)	1 (0.1)
鼻ヘルペス	0	0	0	1 (0.3)	0	0	1 (0.1)

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感染症および寄生虫症 (Cont.)							
上咽頭炎	16 (37.2)	16 (34.8)	32 (36.0)	47 (13.6)	46 (13.1)	11 (7.3)	104 (12.3)
口腔カンジダ症	1 (2.3)	0	1 (1.1)	2 (0.6)	0	1 (0.7)	3 (0.4)
口腔真菌感染	0	0	0	0	1 (0.3)	0	1 (0.1)
口腔ヘルペス	0	0	0	2 (0.6)	3 (0.9)	1 (0.7)	6 (0.7)
外耳炎	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
中耳炎	0	0	0	0	0	1 (0.7)	1 (0.1)
急性中耳炎	0	0	0	1 (0.3)	0	0	1 (0.1)
寄生虫性胃腸炎	0	0	0	0	0	1 (0.7)	1 (0.1)
爪囲炎	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
骨盤膿瘍	0	0	0	0	1 (0.3)	0	1 (0.1)
骨盤内感染	0	0	0	1 (0.3)	0	0	1 (0.1)
骨盤内炎症性疾患	0	0	0	0	1 (0.3)	0	1 (0.1)
歯冠周囲炎	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
会陰膿瘍	0	0	0	1 (0.3)	0	0	1 (0.1)
歯周炎	2 (4.7)	0	2 (2.2)	3 (0.9)	0	0	3 (0.4)
扁桃周囲膿瘍	0	0	0	0	1 (0.3)	0	1 (0.1)
咽頭炎	1 (2.3)	1 (2.2)	2 (2.2)	4 (1.2)	7 (2.0)	6 (4.0)	17 (2.0)

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感染症および寄生虫症 (Cont.)							
レンサ球菌性咽頭炎	0	0	0	4 (1.2)	0	1 (0.7)	5 (0.6)
咽頭扁桃炎	0	0	0	0	1 (0.3)	0	1 (0.1)
肺炎	1 (2.3)	0	1 (1.1)	4 (1.2)	7 (2.0)	1 (0.7)	12 (1.4)
マイコプラズマ性肺炎	0	0	0	0	0	1 (0.7)	1 (0.1)
処置後感染	0	0	0	0	1 (0.3)	0	1 (0.1)
化膿	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
腎盂腎炎	0	0	0	0	0	1 (0.7)	1 (0.1)
急性腎盂腎炎	0	0	0	0	1 (0.3)	0	1 (0.1)
膿疱性皮疹	0	0	0	2 (0.6)	0	0	2 (0.2)
気道感染	0	0	0	0	0	1 (0.7)	1 (0.1)
ウイルス性気道感染	0	0	0	1 (0.3)	0	0	1 (0.1)
鼻炎	0	1 (2.2)	1 (1.1)	3 (0.9)	4 (1.1)	0	7 (0.8)
敗血症	0	0	0	0	0	1 (0.7)	1 (0.1)
副鼻腔炎	1 (2.3)	2 (4.3)	3 (3.4)	14 (4.1)	11 (3.1)	7 (4.6)	32 (3.8)
皮膚カンジダ	0	0	0	0	1 (0.3)	0	1 (0.1)
皮膚感染	0	0	0	0	2 (0.6)	0	2 (0.2)
ブドウ球菌感染	0	0	0	0	1 (0.3)	0	1 (0.1)

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感染症および寄生虫症 (Cont.)							
胸骨炎	0	0	0	1 (0.3)	0	0	1 (0.1)
レンサ球菌感染	0	0	0	1 (0.3)	0	0	1 (0.1)
頭部白癬	0	0	0	1 (0.3)	0	0	1 (0.1)
癜風	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
扁桃炎	1 (2.3)	0	1 (1.1)	3 (0.9)	3 (0.9)	2 (1.3)	8 (0.9)
歯膿瘍	0	0	0	2 (0.6)	0	2 (1.3)	4 (0.5)
歯感染	0	0	0	2 (0.6)	4 (1.1)	0	6 (0.7)
結核	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
胸腔内リンパ節結核	0	0	0	0	1 (0.3)	0	1 (0.1)
上気道感染	1 (2.3)	2 (4.3)	3 (3.4)	22 (6.4)	19 (5.4)	9 (6.0)	50 (5.9)
尿路感染	0	0	0	8 (2.3)	4 (1.1)	4 (2.6)	16 (1.9)
膣感染	0	0	0	1 (0.3)	0	0	1 (0.1)
ウイルス感染	0	0	0	1 (0.3)	2 (0.6)	1 (0.7)	4 (0.5)
ウイルス性咽頭炎	0	0	0	0	2 (0.6)	0	2 (0.2)
外陰部膣カンジダ症	0	0	0	0	3 (0.9)	0	3 (0.4)
外陰膣真菌感染	0	0	0	1 (0.3)	2 (0.6)	1 (0.7)	4 (0.5)
外陰膣炎	0	0	0	0	0	1 (0.7)	1 (0.1)
エルシニア感染	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)

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傷害、中毒および処置合併症	2 (4.7)	2 (4.3)	4 (4.5)	19 (5.5)	18 (5.1)	8 (5.3)	45 (5.3)
動物咬傷	0	0	0	2 (0.6)	0	0	2 (0.2)
足関節部骨折	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
節足動物咬傷	0	0	0	0	0	1 (0.7)	1 (0.1)
節足動物刺傷	0	1 (2.2)	1 (1.1)	1 (0.3)	1 (0.3)	0	2 (0.2)
第2度熱傷	0	0	0	0	0	1 (0.7)	1 (0.1)
術後錯乱	0	0	0	0	1 (0.3)	0	1 (0.1)
挫傷	1 (2.3)	0	1 (1.1)	1 (0.3)	1 (0.3)	0	2 (0.2)
転倒	0	0	0	0	1 (0.3)	0	1 (0.1)
尾骨骨折	0	0	0	0	0	1 (0.7)	1 (0.1)
仙骨骨折	0	0	0	0	1 (0.3)	0	1 (0.1)
上腕骨骨折	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
注射に伴う反応	0	1 (2.2)	1 (1.1)	0	1 (0.3)	1 (0.7)	2 (0.2)
関節脱臼	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
関節損傷	0	0	0	1 (0.3)	0	0	1 (0.1)
靱帯捻挫	0	0	0	2 (0.6)	0	0	2 (0.2)

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傷害、中毒および処置合併症 (Cont.)							
四肢損傷	0	0	0	0	0	1 (0.7)	1 (0.1)
半月板損傷	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
肉離れ	0	0	0	1 (0.3)	0	0	1 (0.1)
膝蓋骨骨折	0	0	0	0	1 (0.3)	0	1 (0.1)
処置後出血	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
術後高血圧	0	0	0	0	1 (0.3)	0	1 (0.1)
処置による疼痛	0	0	0	2 (0.6)	1 (0.3)	0	3 (0.4)
橈骨骨折	0	0	0	0	1 (0.3)	0	1 (0.1)
肋骨骨折	0	0	0	1 (0.3)	0	0	1 (0.1)
交通事故	0	0	0	1 (0.3)	0	0	1 (0.1)
瘢痕	0	0	0	0	1 (0.3)	0	1 (0.1)
皮膚裂傷	0	0	0	2 (0.6)	0	1 (0.7)	3 (0.4)
ストーマ合併症	0	0	0	0	0	1 (0.7)	1 (0.1)
熱傷	0	0	0	0	1 (0.3)	0	1 (0.1)
脛骨骨折	0	0	0	0	1 (0.3)	0	1 (0.1)
上肢骨折	0	0	0	1 (0.3)	0	0	1 (0.1)
創傷	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)

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臨床検査	4 (9.3)	5 (10.9)	9 (10.1)	25 (7.2)	28 (8.0)	12 (7.9)	65 (7.7)
アラニンアミノトランスフェラーゼ増加	0	1 (2.2)	1 (1.1)	2 (0.6)	5 (1.4)	0	7 (0.8)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (2.2)	1 (1.1)	4 (1.2)	7 (2.0)	1 (0.7)	12 (1.4)
抱合ビリルビン増加	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
血中ビリルビン増加	0	1 (2.2)	1 (1.1)	1 (0.3)	2 (0.6)	1 (0.7)	4 (0.5)
血中コレステロール増加	0	0	0	0	0	3 (2.0)	3 (0.4)
血中クレアチニン増加	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
血中ブドウ糖増加	0	0	0	1 (0.3)	0	0	1 (0.1)
血中鉄減少	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
血圧上昇	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
血中甲状腺刺激ホルモン正常	0	0	0	1 (0.3)	0	0	1 (0.1)
血中トリグリセリド増加	0	0	0	0	1 (0.3)	2 (1.3)	3 (0.4)
体温上昇	0	0	0	0	0	1 (0.7)	1 (0.1)
C－反応性蛋白増加	0	0	0	4 (1.2)	2 (0.6)	0	6 (0.7)
心雑音	0	0	0	0	0	1 (0.7)	1 (0.1)
クロストリジウム検査陽性	0	1 (2.2)	1 (1.1)	1 (0.3)	1 (0.3)	0	2 (0.2)
尿中結晶陽性	0	0	0	0	0	1 (0.7)	1 (0.1)

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臨床検査 (Cont.)							
握力低下	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
ヘマトクリット減少	0	0	0	1 (0.3)	0	0	1 (0.1)
ヘモグロビン減少	0	0	0	2 (0.6)	1 (0.3)	0	3 (0.4)
心拍数不整	0	0	0	1 (0.3)	0	0	1 (0.1)
肝酵素上昇	1 (2.3)	0	1 (1.1)	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
HIV検査陽性	0	0	0	0	0	1 (0.7)	1 (0.1)
リパーゼ増加	0	0	0	1 (0.3)	0	0	1 (0.1)
肝機能検査値上昇	0	0	0	3 (0.9)	2 (0.6)	0	5 (0.6)
リンパ球数増加	0	0	0	1 (0.3)	0	0	1 (0.1)
好中球数減少	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
血小板数増加	0	0	0	0	1 (0.3)	0	1 (0.1)
赤血球数減少	0	0	0	1 (0.3)	0	0	1 (0.1)
サイロキシン増加	0	0	0	1 (0.3)	0	0	1 (0.1)
トランスアミナーゼ上昇	0	0	0	0	0	1 (0.7)	1 (0.1)
トリヨードチロニン正常	0	0	0	1 (0.3)	0	0	1 (0.1)
尿検査異常	0	0	0	0	1 (0.3)	0	1 (0.1)
尿中ウロビリノーゲン増加	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)

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臨床検査 (Cont.)							
体重減少	1 (2.3)	1 (2.2)	2 (2.2)	1 (0.3)	2 (0.6)	0	3 (0.4)
体重増加	2 (4.7)	0	2 (2.2)	2 (0.6)	0	0	2 (0.2)
白血球数減少	1 (2.3)	2 (4.3)	3 (3.4)	2 (0.6)	5 (1.4)	3 (2.0)	10 (1.2)
白血球数増加	0	0	0	0	1 (0.3)	0	1 (0.1)
尿中白血球陽性	0	0	0	0	0	1 (0.7)	1 (0.1)
代謝および栄養障害	2 (4.7)	0	2 (2.2)	16 (4.6)	15 (4.3)	4 (2.6)	35 (4.1)
食欲減退	1 (2.3)	0	1 (1.1)	3 (0.9)	2 (0.6)	0	5 (0.6)
脱水	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
糖尿病	1 (2.3)	0	1 (1.1)	2 (0.6)	2 (0.6)	0	4 (0.5)
コントロール不良の糖尿病	0	0	0	1 (0.3)	0	0	1 (0.1)
痛風	0	0	0	0	1 (0.3)	0	1 (0.1)
高カルシウム血症	0	0	0	1 (0.3)	0	0	1 (0.1)
高コレステロール血症	0	0	0	6 (1.7)	2 (0.6)	1 (0.7)	9 (1.1)
高脂血症	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
高トリグリセリド血症	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
低アルブミン血症	0	0	0	0	1 (0.3)	0	1 (0.1)
低カリウム血症	0	0	0	1 (0.3)	4 (1.1)	1 (0.7)	6 (0.7)

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代謝および栄養障害 (Cont.)							
低ナトリウム血症	0	0	0	0	1 (0.3)	0	1 (0.1)
低リン酸血症	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
ビタミン欠乏症	0	0	0	0	1 (0.3)	0	1 (0.1)
血液量減少症	0	0	0	0	0	1 (0.7)	1 (0.1)
空腹時血中ブドウ糖不良	0	0	0	0	0	1 (0.7)	1 (0.1)
鉄欠乏	0	0	0	1 (0.3)	2 (0.6)	1 (0.7)	4 (0.5)
栄養障害	0	0	0	0	1 (0.3)	0	1 (0.1)
代謝性アルカローシス	0	0	0	0	0	1 (0.7)	1 (0.1)
ビタミンB12欠乏	0	0	0	1 (0.3)	0	0	1 (0.1)
ビタミンD欠乏	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
筋骨格系および結合組織障害	4 (9.3)	4 (8.7)	8 (9.0)	49 (14.2)	56 (16.0)	14 (9.3)	119 (14.1)
関節痛	0	1 (2.2)	1 (1.1)	24 (7.0)	25 (7.1)	5 (3.3)	54 (6.4)
関節炎	0	0	0	2 (0.6)	1 (0.3)	2 (1.3)	5 (0.6)
関節障害	0	0	0	0	0	1 (0.7)	1 (0.1)
腋窩腫瘤	0	0	0	0	1 (0.3)	0	1 (0.1)
背部痛	3 (7.0)	1 (2.2)	4 (4.5)	9 (2.6)	10 (2.9)	3 (2.0)	22 (2.6)
尾骨痛	0	0	0	2 (0.6)	0	0	2 (0.2)

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筋骨格系および結合組織障害 (Cont.)							
デュプイトラン拘縮	0	0	0	0	1 (0.3)	0	1 (0.1)
瘻孔	0	0	0	0	1 (0.3)	0	1 (0.1)
側腹部痛	0	0	0	0	0	1 (0.7)	1 (0.1)
単径部痛	0	0	0	1 (0.3)	0	0	1 (0.1)
椎間板変性症	0	0	0	0	2 (0.6)	0	2 (0.2)
椎間板突出	0	0	0	0	1 (0.3)	0	1 (0.1)
関節硬直	0	0	0	1 (0.3)	0	0	1 (0.1)
関節腫脹	0	0	0	0	1 (0.3)	0	1 (0.1)
ループス様症候群	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
運動性低下	0	0	0	1 (0.3)	0	0	1 (0.1)
筋痙縮	0	0	0	4 (1.2)	2 (0.6)	1 (0.7)	7 (0.8)
筋力低下	0	0	0	1 (0.3)	0	0	1 (0.1)
筋骨格系胸痛	0	0	0	0	2 (0.6)	0	2 (0.2)
筋骨格痛	0	0	0	0	3 (0.9)	1 (0.7)	4 (0.5)
筋肉痛	0	0	0	6 (1.7)	4 (1.1)	1 (0.7)	11 (1.3)
筋炎	0	0	0	1 (0.3)	0	0	1 (0.1)
頚部痛	0	0	0	0	2 (0.6)	0	2 (0.2)

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MedDRA 22.0 System Organ Class Preferred Term	Japan Safety Set Adalimumab 40mg EOW (N=43) n (%)	Japan Safety Set Adalimumab 40mg EW (N=46) n (%)	Japan Safety Set Adalimumab Total (N=89) n (%)	Integrated Safety Set Adalimumab 40mg EOW (N=345) n (%)	Integrated Safety Set Adalimumab 40mg EW (N=350) n (%)	Integrated Safety Set Adalimumab TDM Regimen (N=151) n (%)	Integrated Safety Set Adalimumab Total (N=846) n (%)
筋骨格系および結合組織障害 (Cont.)							
変形性関節症	0	0	0	1 (0.3)	0	0	1 (0.1)
骨減少症	0	0	0	0	3 (0.9)	0	3 (0.4)
骨粗鬆症	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
四肢痛	0	0	0	2 (0.6)	9 (2.6)	1 (0.7)	12 (1.4)
顎痛	0	0	0	0	0	1 (0.7)	1 (0.1)
関節周囲炎	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
肩回旋筋腱板症候群	0	0	0	1 (0.3)	0	0	1 (0.1)
仙腸骨炎	0	0	0	0	2 (0.6)	0	2 (0.2)
変形性脊椎症	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
脊椎痛	0	0	0	0	1 (0.3)	0	1 (0.1)
滑液嚢腫	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
滑膜炎	0	0	0	0	1 (0.3)	0	1 (0.1)
顎関節症候群	0	0	0	0	1 (0.3)	0	1 (0.1)
腱痛	0	0	0	0	1 (0.3)	0	1 (0.1)
腱炎	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
斜頚	0	0	0	1 (0.3)	0	0	1 (0.1)

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良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (2.2)	1 (1.1)	5 (1.4)	12 (3.4)	3 (2.0)	20 (2.4)
アクロコルドン	0	0	0	0	2 (0.6)	0	2 (0.2)
肛門性器疣贅	0	0	0	0	1 (0.3)	0	1 (0.1)
基底細胞癌	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
膀胱癌	0	0	0	0	1 (0.3)	0	1 (0.1)
線維腫症	0	0	0	0	1 (0.3)	0	1 (0.1)
胃腸管腺腫	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
脂肪腫	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
悪性黒色腫	0	0	0	0	1 (0.3)	0	1 (0.1)
メラノサイト性母斑	0	0	0	3 (0.9)	0	1 (0.7)	4 (0.5)
新生物	0	0	0	0	1 (0.3)	0	1 (0.1)
非小細胞肺癌	0	0	0	1 (0.3)	0	0	1 (0.1)
食道腺癌	0	0	0	0	1 (0.3)	0	1 (0.1)
脂漏性角化症	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
子宮平滑筋腫	0	0	0	0	1 (0.3)	0	1 (0.1)
神経系障害	4 (9.3)	2 (4.3)	6 (6.7)	31 (9.0)	42 (12.0)	13 (8.6)	86 (10.2)
意識変容状態	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
健忘	0	1 (2.2)	1 (1.1)	0	1 (0.3)	1 (0.7)	2 (0.2)

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神経系障害 (Cont.)							
脳血管障害	0	0	0	0	0	1 (0.7)	1 (0.1)
慢性炎症性脱髄性多発根ニューロパチー	0	0	0	0	0	1 (0.7)	1 (0.1)
注意力障害	0	0	0	0	1 (0.3)	0	1 (0.1)
浮動性めまい	1 (2.3)	0	1 (1.1)	6 (1.7)	5 (1.4)	2 (1.3)	13 (1.5)
体位性めまい	0	0	0	0	1 (0.3)	0	1 (0.1)
頭部不快感	0	0	0	0	1 (0.3)	0	1 (0.1)
頭痛	1 (2.3)	2 (4.3)	3 (3.4)	17 (4.9)	22 (6.3)	8 (5.3)	47 (5.6)
知覚過敏	0	0	0	0	1 (0.3)	0	1 (0.1)
感覚鈍麻	1 (2.3)	0	1 (1.1)	1 (0.3)	4 (1.1)	0	5 (0.6)
虚血性脳卒中	0	0	0	0	0	1 (0.7)	1 (0.1)
腰仙部神経根障害	0	0	0	0	1 (0.3)	0	1 (0.1)
片頭痛	0	0	0	2 (0.6)	5 (1.4)	0	7 (0.8)
単ニューロパチー	0	0	0	0	1 (0.3)	0	1 (0.1)
末梢性ニューロパチー	0	0	0	0	1 (0.3)	0	1 (0.1)
錯感覚	0	0	0	4 (1.2)	2 (0.6)	2 (1.3)	8 (0.9)
坐骨神経痛	0	0	0	3 (0.9)	2 (0.6)	0	5 (0.6)
視野欠損	0	0	0	0	2 (0.6)	0	2 (0.2)

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精神障害	1 (2.3)	3 (6.5)	4 (4.5)	10 (2.9)	13 (3.7)	6 (4.0)	29 (3.4)
抑うつ気分を伴う適応障害	0	0	0	0	1 (0.3)	0	1 (0.1)
激越	0	0	0	0	1 (0.3)	0	1 (0.1)
不安	0	0	0	5 (1.4)	1 (0.3)	2 (1.3)	8 (0.9)
むちゃ飲み	0	0	0	0	0	1 (0.7)	1 (0.1)
双極性障害	0	0	0	0	1 (0.3)	0	1 (0.1)
抑うつ気分	0	0	0	1 (0.3)	0	2 (1.3)	3 (0.4)
うつ病	0	0	0	2 (0.6)	2 (0.6)	1 (0.7)	5 (0.6)
感情的苦悩	0	0	0	0	0	1 (0.7)	1 (0.1)
疾病恐怖	0	0	0	0	0	1 (0.7)	1 (0.1)
不眠症	1 (2.3)	3 (6.5)	4 (4.5)	3 (0.9)	4 (1.1)	1 (0.7)	8 (0.9)
精神疲労	0	0	0	0	0	1 (0.7)	1 (0.1)
落ち着きのなさ	0	0	0	0	1 (0.3)	0	1 (0.1)
睡眠障害	0	0	0	0	1 (0.3)	0	1 (0.1)
ストレス	0	0	0	0	1 (0.3)	0	1 (0.1)
自殺念慮	0	0	0	0	1 (0.3)	0	1 (0.1)

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腎および尿路障害	0	2 (4.3)	2 (2.2)	9 (2.6)	9 (2.6)	3 (2.0)	21 (2.5)
尿路結石	0	1 (2.2)	1 (1.1)	1 (0.3)	1 (0.3)	0	2 (0.2)
排尿困難	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
血尿	0	1 (2.2)	1 (1.1)	1 (0.3)	3 (0.9)	0	4 (0.5)
腎結石症	0	0	0	3 (0.9)	1 (0.3)	2 (1.3)	6 (0.7)
ネフローゼ症候群	0	0	0	1 (0.3)	0	0	1 (0.1)
夜間頻尿	0	0	0	0	1 (0.3)	0	1 (0.1)
頻尿	0	0	0	0	1 (0.3)	0	1 (0.1)
腎前性腎不全	0	0	0	0	1 (0.3)	0	1 (0.1)
腎仙痛	0	0	0	2 (0.6)	0	0	2 (0.2)
腎嚢胞	0	0	0	0	0	1 (0.7)	1 (0.1)
尿失禁	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
尿閉	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
生殖系および乳房障害	1 (2.3)	0	1 (1.1)	8 (2.3)	5 (1.4)	1 (0.7)	14 (1.7)
無月経	0	0	0	0	1 (0.3)	0	1 (0.1)
バルトリン嚢腫	0	0	0	1 (0.3)	0	0	1 (0.1)
乳房腫瘤	0	0	0	0	1 (0.3)	0	1 (0.1)
月経困難症	0	0	0	3 (0.9)	0	1 (0.7)	4 (0.5)

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生殖系および乳房障害 (Cont.)							
卵管障害	0	0	0	1 (0.3)	0	0	1 (0.1)
卵巣嚢胞	0	0	0	1 (0.3)	0	0	1 (0.1)
多嚢胞性卵巣	0	0	0	0	1 (0.3)	0	1 (0.1)
前立腺炎	1 (2.3)	0	1 (1.1)	1 (0.3)	1 (0.3)	0	2 (0.2)
前立腺腫大	0	0	0	1 (0.3)	0	0	1 (0.1)
精索静脈瘤	0	0	0	0	1 (0.3)	0	1 (0.1)
呼吸器、胸郭および縦隔障害	4 (9.3)	4 (8.7)	8 (9.0)	34 (9.9)	44 (12.6)	9 (6.0)	87 (10.3)
喘息	0	0	0	1 (0.3)	0	0	1 (0.1)
咳嗽	0	1 (2.2)	1 (1.1)	8 (2.3)	12 (3.4)	2 (1.3)	22 (2.6)
発声障害	0	0	0	0	1 (0.3)	0	1 (0.1)
呼吸困難	0	0	0	4 (1.2)	2 (0.6)	0	6 (0.7)
肺気腫	0	0	0	0	1 (0.3)	0	1 (0.1)
鼻出血	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
喀血	0	0	0	0	1 (0.3)	0	1 (0.1)
鼻閉	1 (2.3)	0	1 (1.1)	5 (1.4)	4 (1.1)	1 (0.7)	10 (1.2)
鼻汁変色	0	0	0	1 (0.3)	0	0	1 (0.1)
鼻の炎症	0	0	0	0	1 (0.3)	0	1 (0.1)

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呼吸器、胸郭および縦隔障害 (Cont.)							
鼻粘膜潰瘍	0	0	0	0	1 (0.3)	0	1 (0.1)
鼻茸	0	0	0	1 (0.3)	0	0	1 (0.1)
鼻中隔弯曲	0	0	0	0	1 (0.3)	0	1 (0.1)
鼻潰瘍	0	0	0	0	1 (0.3)	0	1 (0.1)
口腔咽頭痛	0	1 (2.2)	1 (1.1)	5 (1.4)	12 (3.4)	5 (3.3)	22 (2.6)
咽頭の炎症	0	0	0	1 (0.3)	0	0	1 (0.1)
胸膜炎	0	0	0	1 (0.3)	0	0	1 (0.1)
湿性咳嗽	0	0	0	0	1 (0.3)	0	1 (0.1)
肺塞栓症	0	0	0	1 (0.3)	3 (0.9)	0	4 (0.5)
肺痛	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
ラ音	0	0	0	1 (0.3)	0	0	1 (0.1)
気道うっ血	0	0	0	1 (0.3)	0	0	1 (0.1)
鼻痛	0	0	0	1 (0.3)	0	0	1 (0.1)
アレルギー性鼻炎	0	1 (2.2)	1 (1.1)	1 (0.3)	4 (1.1)	0	5 (0.6)
鼻漏	0	0	0	1 (0.3)	2 (0.6)	1 (0.7)	4 (0.5)
副鼻腔うっ血	0	0	0	3 (0.9)	3 (0.9)	0	6 (0.7)
副鼻腔ポリープ	0	0	0	1 (0.3)	0	0	1 (0.1)

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呼吸器、胸郭および縦隔障害 (Cont.)							
睡眠時無呼吸症候群	0	0	0	2 (0.6)	0	0	2 (0.2)
上気道の炎症	2 (4.7)	1 (2.2)	3 (3.4)	2 (0.6)	1 (0.3)	0	3 (0.4)
上気道咳症候群	0	0	0	4 (1.2)	1 (0.3)	0	5 (0.6)
喘鳴	0	0	0	0	1 (0.3)	0	1 (0.1)
皮膚および皮下組織障害	6 (14.0)	10 (21.7)	16 (18.0)	50 (14.5)	69 (19.7)	19 (12.6)	138 (16.3)
ざ瘡	0	3 (6.5)	3 (3.4)	7 (2.0)	7 (2.0)	3 (2.0)	17 (2.0)
脱毛症	0	2 (4.3)	2 (2.2)	4 (1.2)	9 (2.6)	3 (2.0)	16 (1.9)
血管浮腫	0	0	0	0	1 (0.3)	0	1 (0.1)
水疱	0	0	0	0	1 (0.3)	0	1 (0.1)
頭部粃糠疹	0	0	0	0	1 (0.3)	0	1 (0.1)
皮膚嚢腫	0	0	0	1 (0.3)	0	0	1 (0.1)
皮膚炎	0	0	0	1 (0.3)	3 (0.9)	0	4 (0.5)
アレルギー性皮膚炎	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
アトピー性皮膚炎	0	0	0	0	1 (0.3)	0	1 (0.1)
接触皮膚炎	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
薬疹	0	0	0	0	1 (0.3)	0	1 (0.1)
皮膚乾燥	0	0	0	2 (0.6)	3 (0.9)	0	5 (0.6)

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皮膚および皮下組織障害 (Cont.)							
斑状出血	0	0	0	1 (0.3)	0	0	1 (0.1)
湿疹	1 (2.3)	1 (2.2)	2 (2.2)	2 (0.6)	4 (1.1)	2 (1.3)	8 (0.9)
紅斑	1 (2.3)	0	1 (1.1)	4 (1.2)	7 (2.0)	2 (1.3)	13 (1.5)
結節性紅斑	0	0	0	2 (0.6)	1 (0.3)	1 (0.7)	4 (0.5)
過剰皮膚	0	0	0	0	1 (0.3)	0	1 (0.1)
剥脱性発疹	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
過角化	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
過敏性血管炎	0	0	0	0	0	1 (0.7)	1 (0.1)
間擦疹	0	0	0	1 (0.3)	0	0	1 (0.1)
扁平苔癬	0	0	0	0	0	1 (0.7)	1 (0.1)
リニアIgA病	0	0	0	1 (0.3)	0	0	1 (0.1)
汗疹	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
爪の障害	0	0	0	0	1 (0.3)	0	1 (0.1)
寝汗	0	0	0	2 (0.6)	2 (0.6)	0	4 (0.5)
掌蹠角皮症	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
類天疱瘡	0	0	0	0	0	1 (0.7)	1 (0.1)
色素沈着障害	0	0	0	0	0	1 (0.7)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）
（統合安全性解析対象集団及び日本人安全性解析対象集団，M14-033 日本サブ試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Japan Safety Set Adalimumab 40mg EOW (N=43) n (%)	Japan Safety Set Adalimumab 40mg EW (N=46) n (%)	Japan Safety Set Total (N=89) n (%)	Integrated Safety Set Adalimumab 40mg EOW (N=345) n (%)	Integrated Safety Set Adalimumab 40mg EW (N=350) n (%)	Integrated Safety Set TDM Regimen (N=151) n (%)	Integrated Safety Set Total (N=846) n (%)
皮膚および皮下組織障害 (Cont.)							
そう痒症	1 (2.3)	1 (2.2)	2 (2.2)	7 (2.0)	9 (2.6)	1 (0.7)	17 (2.0)
乾癬	0	0	0	2 (0.6)	1 (0.3)	1 (0.7)	4 (0.5)
発疹	1 (2.3)	1 (2.2)	2 (2.2)	11 (3.2)	20 (5.7)	4 (2.6)	35 (4.1)
紅斑性皮疹	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
斑状皮疹	0	0	0	0	1 (0.3)	0	1 (0.1)
丘疹性皮疹	0	0	0	2 (0.6)	2 (0.6)	1 (0.7)	5 (0.6)
酒さ	0	0	0	0	1 (0.3)	0	1 (0.1)
脂漏性皮膚炎	0	0	0	0	0	1 (0.7)	1 (0.1)
皮膚灼熱感	0	0	0	1 (0.3)	0	0	1 (0.1)
皮膚病変	0	0	0	2 (0.6)	2 (0.6)	1 (0.7)	5 (0.6)
皮膚線条	0	0	0	0	1 (0.3)	0	1 (0.1)
角層下膿疱性皮膚症	0	0	0	0	1 (0.3)	0	1 (0.1)
顔面腫脹	0	0	0	0	1 (0.3)	0	1 (0.1)
蕁麻疹	0	1 (2.2)	1 (1.1)	1 (0.3)	3 (0.9)	0	4 (0.5)
社会環境	0	0	0	1 (0.3)	0	0	1 (0.1)
閉経	0	0	0	1 (0.3)	0	0	1 (0.1)

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MedDRA 22.0 System Organ Class Preferred Term	Japan Safety Set Adalimumab 40mg EOW (N=43) n (%)	Japan Safety Set Adalimumab 40mg EW (N=46) n (%)	Japan Safety Set Total (N=89) n (%)	Integrated Safety Set Adalimumab 40mg EOW (N=345) n (%)	Integrated Safety Set Adalimumab 40mg EW (N=350) n (%)	Integrated Safety Set TDM Regimen (N=151) n (%)	Integrated Safety Set Total (N=846) n (%)
血管障害	1 (2.3)	2 (4.3)	3 (3.4)	10 (2.9)	14 (4.0)	3 (2.0)	27 (3.2)
大動脈瘤	0	0	0	0	1 (0.3)	0	1 (0.1)
大動脈硬化症	0	0	0	0	1 (0.3)	0	1 (0.1)
動脈炎	0	0	0	0	1 (0.3)	0	1 (0.1)
本態性高血圧症	0	0	0	0	0	1 (0.7)	1 (0.1)
潮紅	0	0	0	0	1 (0.3)	0	1 (0.1)
血腫	0	0	0	0	1 (0.3)	0	1 (0.1)
高血圧	0	1 (2.2)	1 (1.1)	6 (1.7)	7 (2.0)	1 (0.7)	14 (1.7)
高血圧性血管障害	0	0	0	0	1 (0.3)	0	1 (0.1)
高血圧クリーゼ	0	0	0	1 (0.3)	0	0	1 (0.1)
低血圧	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
起立性低血圧	0	0	0	0	0	1 (0.7)	1 (0.1)
蒼白	0	0	0	1 (0.3)	0	0	1 (0.1)
静脈炎	0	0	0	0	1 (0.3)	0	1 (0.1)
血栓性静脈炎	0	1 (2.2)	1 (1.1)	1 (0.3)	1 (0.3)	0	2 (0.2)
血栓症	0	0	0	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）
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Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent adverse events during the maintenance study are defined as events that begin or worsen either on or after the first dose of the study drug in the maintenance study and within 70 days after the last dose of the study drug.

Cross Reference: M14-033 Maintenance Japan Sub-study Final CSR_Table 14.3__1.2.1_J

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）
（統合安全性解析対象集団及び日本人安全性解析対象集団，M14-033 日本サブ試験の維持療法試験）

MedDRA 22.0 System Organ Class Preferred Term	Japan Safety Set Adalimumab 40mg EOW (N=43) n (%)	Japan Safety Set Adalimumab 40mg EW (N=46) n (%)	Japan Safety Set Adalimumab Total (N=89) n (%)	Integrated Safety Set Adalimumab 40mg EOW (N=345) n (%)	Integrated Safety Set Adalimumab 40mg EW (N=350) n (%)	Integrated Safety Set Adalimumab TDM Regimen (N=151) n (%)	Integrated Safety Set Adalimumab Total (N=846) n (%)
Any Adverse Event	7 (16.3)	13 (28.3)	20 (22.5)	89 (25.8)	117 (33.4)	49 (32.5)	255 (30.1)
血液およびリンパ系障害	0	0	0	3 (0.9)	6 (1.7)	4 (2.6)	13 (1.5)
貧血	0	0	0	0	1 (0.3)	0	1 (0.1)
白血球減少症	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
リンパ節症	0	0	0	0	2 (0.6)	1 (0.7)	3 (0.4)
リンパ球減少症	0	0	0	0	0	1 (0.7)	1 (0.1)
好中球減少症	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
血小板減少症	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
血小板増加症	0	0	0	1 (0.3)	0	0	1 (0.1)
耳および迷路障害	0	0	0	4 (1.2)	0	0	4 (0.5)
耳鳴	0	0	0	2 (0.6)	0	0	2 (0.2)
回転性めまい	0	0	0	2 (0.6)	0	0	2 (0.2)
眼障害	0	0	0	3 (0.9)	3 (0.9)	0	6 (0.7)
ドライアイ	0	0	0	0	1 (0.3)	0	1 (0.1)
眼の炎症	0	0	0	0	1 (0.3)	0	1 (0.1)
眼痛	0	0	0	1 (0.3)	0	0	1 (0.1)
眼瞼縁痂皮	0	0	0	0	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）
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眼障害 (Cont.)							
眼瞼下垂	0	0	0	0	1 (0.3)	0	1 (0.1)
視神経萎縮	0	0	0	1 (0.3)	0	0	1 (0.1)
視力障害	0	0	0	1 (0.3)	0	0	1 (0.1)
胃腸障害	1 (2.3)	1 (2.2)	2 (2.2)	10 (2.9)	14 (4.0)	7 (4.6)	31 (3.7)
腹部膨満	0	0	0	2 (0.6)	0	0	2 (0.2)
腹痛	0	0	0	0	1 (0.3)	0	1 (0.1)
上腹部痛	0	0	0	1 (0.3)	0	0	1 (0.1)
裂肛	0	0	0	0	1 (0.3)	0	1 (0.1)
肛門そう痒症	0	0	0	0	0	1 (0.7)	1 (0.1)
アフタ性潰瘍	0	0	0	0	0	1 (0.7)	1 (0.1)
潰瘍性大腸炎	0	0	0	3 (0.9)	6 (1.7)	3 (2.0)	12 (1.4)
クローン病	0	0	0	0	1 (0.3)	0	1 (0.1)
下痢	0	0	0	2 (0.6)	0	0	2 (0.2)
口内乾燥	0	0	0	0	1 (0.3)	0	1 (0.1)
鼓腸	0	0	0	0	0	1 (0.7)	1 (0.1)
歯肉出血	0	0	0	0	1 (0.3)	0	1 (0.1)
舌炎	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）
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胃腸障害 (Cont.)							
血便排泄	0	0	0	1 (0.3)	0	0	1 (0.1)
痔核	0	0	0	0	1 (0.3)	0	1 (0.1)
粘液便	0	0	0	1 (0.3)	0	0	1 (0.1)
悪心	1 (2.3)	0	1 (1.1)	3 (0.9)	1 (0.3)	1 (0.7)	5 (0.6)
急性膵炎	0	0	0	1 (0.3)	0	0	1 (0.1)
肛門周囲痛	0	0	0	1 (0.3)	0	0	1 (0.1)
直腸出血	0	0	0	1 (0.3)	0	0	1 (0.1)
歯痛	0	0	0	0	2 (0.6)	0	2 (0.2)
一般・全身障害および投与部位の状態	1 (2.3)	1 (2.2)	2 (2.2)	15 (4.3)	27 (7.7)	6 (4.0)	48 (5.7)
無力症	0	0	0	3 (0.9)	4 (1.1)	0	7 (0.8)
嚢胞	0	0	0	1 (0.3)	0	0	1 (0.1)
薬物相互作用	0	0	0	0	1 (0.3)	0	1 (0.1)
異形成	0	0	0	0	0	1 (0.7)	1 (0.1)
疲労	0	0	0	2 (0.6)	2 (0.6)	0	4 (0.5)
高熱	0	0	0	0	0	1 (0.7)	1 (0.1)
インフルエンザ様疾患	0	0	0	0	2 (0.6)	0	2 (0.2)
注入部位紅斑	0	0	0	0	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）
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一般・全身障害および投与部位の状態 (Cont.)							
注入部位そう痒感	0	0	0	0	1 (0.3)	0	1 (0.1)
注射部位紅斑	0	0	0	3 (0.9)	2 (0.6)	1 (0.7)	6 (0.7)
注射部位過敏反応	0	0	0	0	1 (0.3)	0	1 (0.1)
注射部位硬結	0	0	0	1 (0.3)	0	0	1 (0.1)
注射部位炎症	0	0	0	0	2 (0.6)	0	2 (0.2)
注射部位結節	0	0	0	1 (0.3)	0	0	1 (0.1)
注射部位疼痛	0	0	0	2 (0.6)	1 (0.3)	0	3 (0.4)
注射部位そう痒感	0	0	0	0	2 (0.6)	1 (0.7)	3 (0.4)
注射部位発疹	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
注射部位反応	0	1 (2.2)	1 (1.1)	2 (0.6)	3 (0.9)	3 (2.0)	8 (0.9)
注射部位腫脹	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
限局性浮腫	0	0	0	1 (0.3)	0	0	1 (0.1)
浮腫	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
末梢腫脹	0	0	0	0	1 (0.3)	0	1 (0.1)
発熱	0	0	0	0	4 (1.1)	0	4 (0.5)
腫脹	0	0	0	0	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）
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肝胆道系障害	1 (2.3)	0	1 (1.1)	3 (0.9)	1 (0.3)	4 (2.6)	8 (0.9)
肝胆道系疾患	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
高トランスアミナーゼ血症	0	0	0	1 (0.3)	1 (0.3)	4 (2.6)	6 (0.7)
非アルコール性脂肪性肝炎	0	0	0	1 (0.3)	0	0	1 (0.1)
感染症および寄生虫症	3 (7.0)	4 (8.7)	7 (7.9)	34 (9.9)	40 (11.4)	20 (13.2)	94 (11.1)
四肢膿瘍	0	0	0	0	2 (0.6)	0	2 (0.2)
急性副鼻腔炎	0	0	0	0	1 (0.3)	0	1 (0.1)
細菌性膣症	0	0	0	0	1 (0.3)	0	1 (0.1)
カンジダ感染	0	0	0	0	1 (0.3)	0	1 (0.1)
蜂巣炎	0	0	0	0	0	1 (0.7)	1 (0.1)
クロストリジウム・ディフィシレ感染	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
結膜炎	0	0	0	0	0	2 (1.3)	2 (0.2)
膀胱炎	0	2 (4.3)	2 (2.2)	1 (0.3)	2 (0.6)	2 (1.3)	5 (0.6)
サイトメガロウイルス感染	0	0	0	1 (0.3)	0	0	1 (0.1)
耳感染	0	0	0	2 (0.6)	0	0	2 (0.2)
エプスタイン・バーウイルス感染	0	0	0	1 (0.3)	0	0	1 (0.1)
外耳蜂巣炎	0	0	0	1 (0.3)	0	0	1 (0.1)
毛包炎	0	0	0	0	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）
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感染症および寄生虫症 (Cont.)							
真菌感染	0	0	0	1 (0.3)	0	0	1 (0.1)
皮膚真菌感染	0	0	0	1 (0.3)	0	1 (0.7)	2 (0.2)
胃腸炎	0	0	0	0	1 (0.3)	0	1 (0.1)
性器カンジダ症	0	0	0	0	1 (0.3)	0	1 (0.1)
歯肉膿瘍	0	0	0	0	1 (0.3)	0	1 (0.1)
ヘルペス眼感染	0	0	0	0	1 (0.3)	0	1 (0.1)
帯状疱疹	0	0	0	3 (0.9)	2 (0.6)	1 (0.7)	6 (0.7)
麦粒腫	0	0	0	0	1 (0.3)	0	1 (0.1)
インフルエンザ	1 (2.3)	1 (2.2)	2 (2.2)	2 (0.6)	6 (1.7)	1 (0.7)	9 (1.1)
下気道感染	0	0	0	0	0	1 (0.7)	1 (0.1)
鼓膜炎	0	0	0	0	0	1 (0.7)	1 (0.1)
上咽頭炎	0	1 (2.2)	1 (1.1)	6 (1.7)	10 (2.9)	5 (3.3)	21 (2.5)
口腔カンジダ症	1 (2.3)	0	1 (1.1)	2 (0.6)	0	0	2 (0.2)
口腔真菌感染	0	0	0	0	1 (0.3)	0	1 (0.1)
口腔ヘルペス	0	0	0	0	2 (0.6)	0	2 (0.2)
外耳炎	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
急性中耳炎	0	0	0	1 (0.3)	0	0	1 (0.1)

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感染症および寄生虫症 (Cont.)							
咽頭炎	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
レンサ球菌性咽頭炎	0	0	0	1 (0.3)	0	0	1 (0.1)
肺炎	1 (2.3)	0	1 (1.1)	2 (0.6)	3 (0.9)	1 (0.7)	6 (0.7)
腎盂腎炎	0	0	0	0	0	1 (0.7)	1 (0.1)
急性腎盂腎炎	0	0	0	0	1 (0.3)	0	1 (0.1)
膿疱性皮疹	0	0	0	2 (0.6)	0	0	2 (0.2)
鼻炎	0	0	0	1 (0.3)	0	0	1 (0.1)
敗血症	0	0	0	0	0	1 (0.7)	1 (0.1)
副鼻腔炎	0	0	0	1 (0.3)	2 (0.6)	2 (1.3)	5 (0.6)
皮膚感染	0	0	0	0	1 (0.3)	0	1 (0.1)
扁桃炎	0	0	0	0	3 (0.9)	1 (0.7)	4 (0.5)
歯膿瘍	0	0	0	1 (0.3)	0	0	1 (0.1)
歯感染	0	0	0	0	1 (0.3)	0	1 (0.1)
結核	0	0	0	0	1 (0.3)	0	1 (0.1)
上気道感染	0	0	0	7 (2.0)	4 (1.1)	3 (2.0)	14 (1.7)
尿路感染	0	0	0	1 (0.3)	1 (0.3)	2 (1.3)	4 (0.5)
膣感染	0	0	0	1 (0.3)	0	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）
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感染症および寄生虫症 (Cont.)							
ウイルス感染	0	0	0	0	1 (0.3)	0	1 (0.1)
ウイルス性咽頭炎	0	0	0	0	2 (0.6)	0	2 (0.2)
外陰部腟カンジダ症	0	0	0	0	1 (0.3)	0	1 (0.1)
外陰腟真菌感染	0	0	0	0	1 (0.3)	0	1 (0.1)
外陰腟炎	0	0	0	0	0	1 (0.7)	1 (0.1)
傷害、中毒および処置合併症	0	1 (2.2)	1 (1.1)	0	1 (0.3)	1 (0.7)	2 (0.2)
注射に伴う反応	0	1 (2.2)	1 (1.1)	0	1 (0.3)	1 (0.7)	2 (0.2)
臨床検査	0	0	0	5 (1.4)	8 (2.3)	3 (2.0)	16 (1.9)
アラニンアミノトランスフェラーゼ増加	0	0	0	0	3 (0.9)	0	3 (0.4)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	0	4 (1.1)	0	4 (0.5)
抱合ビリルビン増加	0	0	0	0	1 (0.3)	0	1 (0.1)
血中ビリルビン増加	0	0	0	0	1 (0.3)	0	1 (0.1)
血中コレステロール増加	0	0	0	0	0	1 (0.7)	1 (0.1)
血中クレアチニン増加	0	0	0	1 (0.3)	0	0	1 (0.1)
血中トリグリセリド増加	0	0	0	0	0	1 (0.7)	1 (0.1)
肝機能検査値上昇	0	0	0	2 (0.6)	0	0	2 (0.2)
好中球数減少	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
白血球数減少	0	0	0	1 (0.3)	3 (0.9)	2 (1.3)	6 (0.7)

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代謝および栄養障害	0	0	0	5 (1.4)	1 (0.3)	0	6 (0.7)
食欲減退	0	0	0	1 (0.3)	0	0	1 (0.1)
コントロール不良の糖尿病	0	0	0	1 (0.3)	0	0	1 (0.1)
高コレステロール血症	0	0	0	1 (0.3)	0	0	1 (0.1)
高トリグリセリド血症	0	0	0	1 (0.3)	0	0	1 (0.1)
低カリウム血症	0	0	0	0	1 (0.3)	0	1 (0.1)
低リン酸血症	0	0	0	1 (0.3)	0	0	1 (0.1)
筋骨格系および結合組織障害	1 (2.3)	1 (2.2)	2 (2.2)	12 (3.5)	17 (4.9)	3 (2.0)	32 (3.8)
関節痛	0	0	0	9 (2.6)	10 (2.9)	2 (1.3)	21 (2.5)
関節炎	0	0	0	0	1 (0.3)	0	1 (0.1)
デュプイトラン拘縮	0	0	0	0	1 (0.3)	0	1 (0.1)
関節硬直	0	0	0	1 (0.3)	0	0	1 (0.1)
関節腫脹	0	0	0	0	1 (0.3)	0	1 (0.1)
ループス様症候群	0	1 (2.2)	1 (1.1)	0	1 (0.3)	0	1 (0.1)
筋痙縮	0	0	0	0	1 (0.3)	0	1 (0.1)
筋骨格系胸痛	0	0	0	0	1 (0.3)	0	1 (0.1)

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筋骨格系および結合組織障害 (Cont.)							
筋肉痛	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
筋炎	0	0	0	1 (0.3)	0	0	1 (0.1)
骨減少症	0	0	0	0	1 (0.3)	0	1 (0.1)
骨粗鬆症	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
四肢痛	0	0	0	2 (0.6)	3 (0.9)	0	5 (0.6)
腱痛	0	0	0	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）	0	0	0	0	5 (1.4)	0	5 (0.6)
アクロコルドン	0	0	0	0	2 (0.6)	0	2 (0.2)
肛門性器疣贅	0	0	0	0	1 (0.3)	0	1 (0.1)
基底細胞癌	0	0	0	0	1 (0.3)	0	1 (0.1)
線維腫症	0	0	0	0	1 (0.3)	0	1 (0.1)
神経系障害	1 (2.3)	1 (2.2)	2 (2.2)	4 (1.2)	13 (3.7)	6 (4.0)	23 (2.7)
意識変容状態	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
健忘	0	1 (2.2)	1 (1.1)	0	1 (0.3)	1 (0.7)	2 (0.2)
慢性炎症性脱髄性多発根ニューロパチー	0	0	0	0	0	1 (0.7)	1 (0.1)
注意力障害	0	0	0	0	1 (0.3)	0	1 (0.1)
浮動性めまい	0	0	0	2 (0.6)	2 (0.6)	1 (0.7)	5 (0.6)

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神経系障害 (Cont.)							
体位性めまい	0	0	0	0	1 (0.3)	0	1 (0.1)
頭部不快感	0	0	0	0	1 (0.3)	0	1 (0.1)
頭痛	0	0	0	0	8 (2.3)	3 (2.0)	11 (1.3)
感覚鈍麻	0	0	0	0	2 (0.6)	0	2 (0.2)
単ニューロパチー	0	0	0	0	1 (0.3)	0	1 (0.1)
錯感覚	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
精神障害	1 (2.3)	1 (2.2)	2 (2.2)	1 (0.3)	3 (0.9)	0	4 (0.5)
激越	0	0	0	0	1 (0.3)	0	1 (0.1)
うつ病	0	0	0	0	1 (0.3)	0	1 (0.1)
不眠症	1 (2.3)	1 (2.2)	2 (2.2)	1 (0.3)	1 (0.3)	0	2 (0.2)
腎および尿路障害	0	0	0	2 (0.6)	0	1 (0.7)	3 (0.4)
腎結石症	0	0	0	1 (0.3)	0	0	1 (0.1)
ネフローゼ症候群	0	0	0	1 (0.3)	0	0	1 (0.1)
尿閉	0	0	0	0	0	1 (0.7)	1 (0.1)
生殖系および乳房障害	0	0	0	1 (0.3)	0	0	1 (0.1)
バルトリン嚢腫	0	0	0	1 (0.3)	0	0	1 (0.1)

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呼吸器、胸郭および縦隔障害	0	0	0	5 (1.4)	11 (3.1)	5 (3.3)	21 (2.5)
咳嗽	0	0	0	3 (0.9)	4 (1.1)	0	7 (0.8)
呼吸困難	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.2)
肺気腫	0	0	0	0	1 (0.3)	0	1 (0.1)
鼻出血	0	0	0	0	1 (0.3)	0	1 (0.1)
鼻閉	0	0	0	0	0	1 (0.7)	1 (0.1)
口腔咽頭痛	0	0	0	0	3 (0.9)	3 (2.0)	6 (0.7)
湿性咳嗽	0	0	0	0	1 (0.3)	0	1 (0.1)
鼻痛	0	0	0	1 (0.3)	0	0	1 (0.1)
鼻漏	0	0	0	0	1 (0.3)	1 (0.7)	2 (0.2)
喘鳴	0	0	0	0	1 (0.3)	0	1 (0.1)
皮膚および皮下組織障害	2 (4.7)	3 (6.5)	5 (5.6)	22 (6.4)	34 (9.7)	13 (8.6)	69 (8.2)
ざ瘡	0	0	0	2 (0.6)	2 (0.6)	2 (1.3)	6 (0.7)
脱毛症	0	0	0	2 (0.6)	6 (1.7)	3 (2.0)	11 (1.3)
皮膚炎	0	0	0	0	1 (0.3)	0	1 (0.1)
アトピー性皮膚炎	0	0	0	0	1 (0.3)	0	1 (0.1)
接触皮膚炎	0	0	0	0	1 (0.3)	0	1 (0.1)
薬疹	0	0	0	0	1 (0.3)	0	1 (0.1)

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皮膚および皮下組織障害 (Cont.)							
皮膚乾燥	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)
湿疹	0	1 (2.2)	1 (1.1)	1 (0.3)	4 (1.1)	1 (0.7)	6 (0.7)
紅斑	0	0	0	2 (0.6)	2 (0.6)	2 (1.3)	6 (0.7)
結節性紅斑	0	0	0	1 (0.3)	0	0	1 (0.1)
剥脱性発疹	0	0	0	1 (0.3)	0	0	1 (0.1)
過角化	1 (2.3)	0	1 (1.1)	1 (0.3)	0	0	1 (0.1)
扁平苔癬	0	0	0	0	0	1 (0.7)	1 (0.1)
リニアIgA病	0	0	0	1 (0.3)	0	0	1 (0.1)
寝汗	0	0	0	0	1 (0.3)	0	1 (0.1)
類天疱瘡	0	0	0	0	0	1 (0.7)	1 (0.1)
そう痒症	0	0	0	2 (0.6)	5 (1.4)	0	7 (0.8)
乾癬	0	0	0	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
発疹	1 (2.3)	1 (2.2)	2 (2.2)	7 (2.0)	11 (3.1)	4 (2.6)	22 (2.6)
紅斑性皮疹	0	0	0	0	1 (0.3)	0	1 (0.1)
丘疹性皮疹	0	0	0	0	1 (0.3)	0	1 (0.1)
皮膚病変	0	0	0	2 (0.6)	1 (0.3)	1 (0.7)	4 (0.5)
角層下膿疱性皮膚症	0	0	0	0	1 (0.3)	0	1 (0.1)
蕁麻疹	0	1 (2.2)	1 (1.1)	0	3 (0.9)	0	3 (0.4)

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血管障害	0	0	0	1 (0.3)	3 (0.9)	0	4 (0.5)
血腫	0	0	0	0	1 (0.3)	0	1 (0.1)
高血圧	0	0	0	1 (0.3)	2 (0.6)	0	3 (0.4)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent adverse events during the maintenance study are defined as events that begin or worsen either on or after the first dose of the study drug in the maintenance study and within 70 days after the last dose of the study drug.
Event with unknown relationship to study drug is being counted as drug-related.

Cross reference: M14-033 Maintenance Japan Sub-study Final CSR_Table 14.3__1.6_J

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ABDOMINAL PAIN	20[redacted]
ANEMIA: LOW LAB VALUES	20[redacted]
ARTHRITIS: JOINT AND LOWER BACK PAIN	20[redacted]
OTHER: SARCOIDOSIS	20[redacted]
MIGRAINE HEADACHE	20[redacted]
OTHER: PERTUSSIS	20[redacted]
COGNITIVE OR PSYCHIATRIC DISORDER: ANXIETY	20[redacted]
EYE DISEASE/DISORDER: CATARACT SURGERY BOTH EYES	20[redacted]
OTHER: VITAMIN D DEFICIENCY	20[redacted]
SLEEP APNEA: INSOMNIA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 148	93

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	10 mg/kg (milligram(s)/kilogram)	Other: Q 6 WEEKS	Y-M: 20[redacted]-[redacted]
PARACETAMOL	750 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted]
LOPERAMIDE	1 TABLET	PRN	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	10 mg/kg (milligram(s)/kilogram)	Other: Q 6 WEEKS	Y-M: 20[redacted]-[redacted] / -336
TRAZODONE	50 mg (milligram(s))	Other: QHS	Y-M: 20[redacted]-[redacted] / -248
DULOXETINE	30 mg (milligram(s))	Other: QHS	Y-M: 20[redacted]-[redacted] / -145
SULFASALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -145
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -62
FENTANYL	100 mcg (microgram(s))	QD	Y-M: 20[redacted]-[redacted] / -5
MIDAZOLAM	7.0 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -5

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	750 mg (milligram(s))	PRN	Y-M: 20[redacted]	ONGOING
LOPERAMIDE	1 TABLET	PRN	Y-M: 20[redacted]	ONGOING
DULOXETINE	30 mg (milligram(s))	Other: QHS	Y-M: 20[redacted] / -145	ONGOING
SULFASALAZINE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -145	ONGOING
DICYCLOVERINE	10 mg (milligram(s))	PRN	Y-M: 20[redacted] / 56	ONGOING
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 56	ONGOING
IRON	325 mg (milligram(s))	BID	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 126

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

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 155 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 167): TOTAL COLECTOMY: COMPLETED SURGERY NO COMPLICATIONS

AE Stopped Rx Day	167 (19 DAYS AFTER LAST TREATMENT)
Duration of AE	13 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	EXACERBATION OF ULCERATIVE COLITIS REQUIRING COLECTOMY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（米国）であり，重篤な有害事象の潰瘍性大腸炎の増悪が認められた。関連する病歴は，炎症性腸疾患及び腹痛であった。被験者は非喫煙者であり，アルコール摂取者（1 日当たり 2 ドリンク未満）であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，結腸全摘術が実施され，合併症はみられなかった。本事象により治験薬の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

6-MERCAPTOPURINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

FERROUS SULFATE for ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: Exacerbation of ulcerative colitis requiring colectomy

- AbbVie: Event is more likely related to pre-existing ulcerative colitis.

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
肺塞栓症	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	4[redacted]	FEMALE	Black

Medical History	Onset Year
DIVERTICULITIS: DIVERTICULOSIS	20[redacted]
OTHER: FATTY LIVER	20[redacted]
OTHER: UTERINE FIBROID TUMOR	20[redacted]
OTHER: BIOPSY OF LEFT BREAST / BENIGN	20[redacted]
ANEMIA: LOW HGB DUE TO UC ANEMIA	20[redacted]
OTHER: NAUSEA	20[redacted]
HYPERTENSION	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 264	208

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 mg (milligram(s))	QD	Y-M: 20[redacted]
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -55
FENTANYL	100 mcg (microgram(s))	Other: ONE TIME	Y-M: 20[redacted] / -22
MIDAZOLAM	5 mg (milligram(s))	Other: ONE TIME	Y-M: 20[redacted] / -22
SODIUM CHLORIDE	1000 mL (millilitre(s))	Other: ONE TIME	Y-M: 20[redacted] / -22

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
MESALAZINE	4.8 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
EVRA	1 PATCH	Other: EVERY 3 WEEKS	Y-M: 20[redacted] / 172	ONGOING
HEPARIN	250 mL (millilitre(s))	Other: ONE TIME	Y-M: 20[redacted] / 267	Y-M: 20[redacted] / 267
HEPARIN	6500 UNITS	Other: ONE TIME	Y-M: 20[redacted] / 267	Y-M: 20[redacted] / 267
IOHEXOL	350 mg (milligram(s))	Other: ONE TIME	Y-M: 20[redacted] / 267	Y-M: 20[redacted] / 267
RIVAROXABAN	15 mg (milligram(s))	BID	Y-M: 20[redacted] / 268	Y-M: 20[redacted] / 289

Event #1: Serious Adverse Event

Event Description	PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 267 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	270 (6 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	POSSIBILITY OF SECONDARY TO ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（米国）であり，重篤な有害事象の肺塞栓症が認められた。関連する病歴は，潰瘍性大腸炎，脂肪肝，及び高血圧であった。
20[redacted] 年 [redacted] 月 [redacted] 日，肺塞栓症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，肺塞栓症は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸痛，息切れ，及び動悸のため病院を受診した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は救急治療室を受診し，同日に肺塞栓症と診断され入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬としてヘパリン，Lohexol，及び Xarelto（リバーロキサバン）が投与された。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([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 HUMIRA (Open Label)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.20.0] [10037377]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of PULMONARY EMBOLISM

- Investigator: POSSIBILITY OF SECONDARY TO ULCERATIVE COLITIS

- AbbVie: PULMONARY EMBOLISM MAY BE ASSOCIATED WITH ULCERATIVE COLITIS.

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
うっ血性心不全	X			
クロストリジウム・ディフィシレ感染		X		
脱水	X			
冠動脈疾患	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	6[redacted]	MALE	White

Medical History	Onset Year
HYPERTENSION	19[redacted]
DIABETES MELLITUS	19[redacted]
HYPERLIPIDEMIA: HIGH CHOLESTEROL	19[redacted]
CORONARY ARTERY DISEASE: TRIPLE BY PASS SURGERY	20[redacted]
OTHER: THROMBOCYTOPENIA	20[redacted]
DEPRESSION: ANXIETY	20[redacted]
OTHER: DEEP VEIN THROMBOSIS	20[redacted]
MYOCARDIAL INFARCTION	20[redacted]
OTHER: ATOPIC DERMATITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 189	133

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
VITAMINS NOS	1 TAB	QD	Y-M: 20[redacted]-[redacted]
METOPROLOL	100 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -344
RANOLAZINE	500 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -344
SIMVASTATIN	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -344
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -285
MESALAZINE	1.2 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / -275
MESALAZINE	60 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / -275
INSULIN GLARGINE	30 mg/kg (milligram(s)/kilogram)	QD	Y-M: 20[redacted]-[redacted] / -253
METFORMIN	500 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -253
GLIPIZIDE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -132
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -83
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -70
FLEET	4.5 OUNCES	Other: ONE TIME	Y-M: 20[redacted]-[redacted] / -6
LIDOCAINE	50 mg (milligram(s))	Other: ONE TIME	Y-M: 20[redacted]-[redacted] / -6
OXYGEN	4 L (litre(s))	Other: ONE TIME	Y-M: 20[redacted]-[redacted] / -6
PROPOFOL	150 mg (milligram(s))	Other: ONE TIME	Y-M: 20[redacted]-[redacted] / -6
SODIUM CHLORIDE	1000 CC	Other: ONE TIME	Y-M: 20[redacted]-[redacted] / -6

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
VITAMINS NOS	1 TAB	QD	Y-M: 20[redacted]	ONGOING
METOPROLOL	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -344	ONGOING
RANOLAZINE	500 mg (milligram(s))	QD	Y-M: 20[redacted] / -344	ONGOING
SIMVASTATIN	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -344	ONGOING
MESALAZINE	1.2 g (gram(s))	QD	Y-M: 20[redacted] / -275	ONGOING
INSULIN GLARGINE	30 mg/kg (milligram(s)/kilogram)	QD	Y-M: 20[redacted] / -253	ONGOING
METFORMIN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / -253	ONGOING
GLIPIZIDE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -132	ONGOING
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -70	ONGOING
ACETYLSALICYLIC ACID	81 mg (milligram(s))	QD	Y-M: 20[redacted] / 43	ONGOING
PARACETAMOL	650 mg (milligram(s))	PRN	Y-M: 20[redacted] / 43	ONGOING
INSULIN LISPRO	100 IU (international unit(s))	TID	Y-M: 20[redacted] / 49	ONGOING
LISINOPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 49	ONGOING
NAPROXEN	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 49	ONGOING
FUROSEMIDE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 173	Y-M: 20[redacted] / 173
I.V. SOLUTIONS	UNKNOWN L (litre(s))	QD	Y-M: 20[redacted] / 173	Y-M: 20[redacted] / 175
FUROSEMIDE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 174	ONGOING
SIMVASTATIN	10 mg (milligram(s))	Other: QHS	Y-M: 20[redacted] / 174	ONGOING
SPIRONOLACTONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 174	ONGOING
VANCOMYCIN	125 mg (milligram(s))	QID	Y-M: 20[redacted]	Y-M: 20[redacted] /

			/ 194	215
I.V. SOLUTIONS	UNKNOWN L (litre(s))	QD	Y-M: 20[redacted] / 195	Y-M: 20[redacted] / 200
ATORVASTATIN	40 mg (milligram(s))	Other: QHS	Y-M: 20[redacted] / 219	ONGOING
GLYCERYL TRINITRATE	0.4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 219	ONGOING
TICAGRELOR	90 mg (milligram(s))	BID	Y-M: 20[redacted] / 219	ONGOING
BUDESONIDE	9 mg/kg (milligram(s)/kilogram)	QD	Y-M: 20[redacted] / 223	ONGOING
MESALAZINE	60 mL (millilitre(s))	Other: QHS	Y-M: 20[redacted] / 223	ONGOING

Event #1: Serious Adverse Event

Event Description	CONGESTIVE HEART FAILURE
Preferred term	うっ血性心不全
AE Onset Date / Rx Day	[redacted]20[redacted] / 173
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 174): TRANSTHORACIC ECHOCARDIOGRAPHY: FLUID REMOVED, DILATATION, RECOVERED	
AE Stopped Rx Day	175
Duration of AE	3 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	VENTRICULAR BLOCKAGE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	CLOSTRIDIUM DIFFICILE
Preferred term	クロストリジウム・ディフィシレ感染

AE Onset Date / Rx Day	[redacted]20[redacted] / 190 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #3: Serious Adverse Event

Event Description	DEHYDRATION
Preferred term	脱水
AE Onset Date / Rx Day	[redacted]20[redacted] / 195 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
[redacted]20[redacted] (RX DAY 190): Stool CLOSTRIDIUM DIFFICILE: P-TOXIN B GENE DETECTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 198): CT OF ABDOMEN: ACTIVE COLITIS RECTOSIGMOID COLON	
AE Stopped Rx Day	200 (11 DAYS AFTER LAST TREATMENT)
Duration of AE	6 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	DEHYDRATION CAUSING CHEST PAIN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #4: Serious Adverse Event

Event Description	CORONARY ARTERY DISEASE
Preferred term	冠動脈疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 217 (28 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	

[redacted]20[redacted] (RX DAY 217): CORONARY CATHETERIZATION: ABNORMAL FINDINGS REQUIRING THE ANGIOPLASTY; ANGIOPLASTY: RESOLVED, STENT PLACED; [redacted]20[redacted] (RX DAY 218): CARDIAC ENZYMES: 16.34 - MYOCARDIAL INJURY, STENT PLACED; [redacted]20[redacted] (RX DAY 219): STRESS TEST: SCAR WITHOUT ISCHEMIA; ELECTROCARDIOGRAM: ECG ABNORMAL, STENT PLACED; [redacted]20[redacted] (RX DAY 220): ECHOCARDIOGRAM: SYSTOLIC FUNCTION REDUCED, STENT PLACED

AE Stopped Rx Day	220 (31 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UNSURE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted]歳の男性（米国）であり，重篤な有害事象のうっ血性心不全が認められた。20[redacted]年[redacted]月[redacted]日，うっ血性心不全が認められた。20[redacted]年[redacted]月[redacted]日，うっ血性心不全は回復した。20[redacted]年[redacted]月[redacted]日，被験者は，うっ血性心不全及び両側肺底部の継続性ラ音のため入院した。20[redacted]年[redacted]月[redacted]日，経胸壁心エコーが実施され，除水後に拡張処置が施された。また，投薬による治療も行われた。20[redacted]年[redacted]月[redacted]日，被験者は退院した。

治療薬として Aldactone（スピロノラクトン）及び Lasix（フロセミド）が投与された。

Causality for HUMIRA (Blinded)

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1) Congestive heart failure (10010684) (Cardiac failure congestive (10007559)) [v.21.0] [10010684]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of CONGESTIVE HEART FAILURE

- Investigator: VENTRICULAR BLOCKAGE

- AbbVie: EVENT MORE LIKELY RELATED TO PRE-EXISTING HYPERTENSION, DIABETES MELLITUS, AND CORONARY ARTERY DISEASE.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（米国）であり，重篤な有害事象の脱水が認められた。関連する病歴は，高血圧，糖尿病，不安，潰瘍性大腸炎，及び冠動脈疾患であった。被験者は非喫煙者であり，軽度のアルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，脱水が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，脱水は回復した。

本事象の発現前には，20[redacted] 年 [redacted] 月 2 日にうっ血性心不全が認められ，20[redacted] 年 [redacted] 月 [redacted] 日に回復している。また，20[redacted] 年 [redacted] 月 [redacted] 日から，クロストリジウム・ディフィシレ感染（非重篤）が認められていた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は脱水及びクロストリジウム・ディフィシレ感染に続発する悪心のため入院した。その他の症状は，浮動性めまい及び下痢であった。治療として輸液及び抗生剤投与が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療として静脈内輸液が実施された。

Causality for HUMIRA (Blinded)

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1) Dehydration (10012174) (Dehydration (10012174)) [v.21.0] [10012174]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし
Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of DEHYDRATION

- Investigator: Dehydration causing chest pain.

- AbbVie: Event more likely secondary to clostridium difficile. Pre-existing ulcerative colitis and diuretic therapy are additional risk factors.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CLOSTRIDIUM DIFFICILE (STOOL): Positive: Toxin B gene detected

[redacted] 20[redacted] CT OF ABDOMEN: Active colitis rectosigmoid colon
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（米国）であり，重篤な有害事象の冠動脈疾患が認められた。関連する病歴は，高血圧，糖尿病，高コレステロール，血小板減少症，三枝血管バイパス術，深部静脈血栓症，及び心筋梗塞であった。被験者は非喫煙者であり，アルコール摂取者（1 日当たり 2 ドリンク未満）であった。
20[redacted] 年[redacted] 月[redacted] 日，冠動脈疾患が認められた。20[redacted] 年[redacted] 月[redacted] 日，冠動脈疾患は回復した。
本事象の発現前には，20[redacted] 年[redacted] 月[redacted] 日から 20[redacted] 年[redacted] 月[redacted] 日の間にうっ血性心不全が認められた。
20[redacted] 年[redacted] 月[redacted] 日，被験者は疲労及び呼吸困難の症状を伴う冠動脈疾患のため入院した。20[redacted] 年[redacted] 月[redacted] 日，血管形成が実施され，本事象は回復した。本事象に関連する家族歴はない。
治療薬としてニトログリセリン及びチカグレロルが投与された。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

IV FLUIDS for DEHYDRATION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

VANCOMYCIN for CLOSTRIDIUM DIFFICILE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Coronary artery disease (10011078) (Coronary artery disease (10011078)) [v.21.1] [10011078]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of CORONARY ARTERY DISEASE

- Investigator: Unsure.

- AbbVie: Risk factors include pre-existing hypertension and diabetes, as well as history of triple bypass surgery and myocardial infarction.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CARDIAC ENZYMES: Troponin elevated at 16.34 (normal range 0-0.01 ng/ml) - myocardial injury

[redacted] 20[redacted] CORONARY CATHETERIZATION: Abnormal findings requiring the Angioplasty

[redacted] 20[redacted] ECHOCARDIOGRAM: systolic function reduced. Right ventricle systolic function reduced.

[redacted] 20[redacted] ELECTROCARDIOGRAM: ECG abnormal. Right bundle block branch block on screening ECG.

[redacted] 20[redacted] ELECTROCARDIOGRAM (SCREENING): Abnormal T waves

[redacted] 20[redacted] STRESS TEST: Scar without ischemia

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
潰瘍性大腸炎	X	X		
門脈脾静脈腸間膜静脈血栓症	X			
小腸閉塞	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	5[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: TONSILLECTOMY	19[redacted]
OTHER: MYOPIA	19[redacted]
OTHER: FATIGUE	19[redacted]
OTHER: INTERMITTENT HEADACHE	19[redacted]
OTHER: WEIGHT LOSS	19[redacted]
OTHER: JOINT PAIN	19[redacted]
OTHER: RIGHT ANKLE FIXATION	19[redacted]
OTHER: INTERMITTENT SINUS CONGESTIN	20[redacted]
OTHER: TORN LIGAMENT RIGHT KNEE	20[redacted]
OTHER: INTERMITTENT DEHYDRATION	20[redacted]
OTHER: MENOPAUSE	20[redacted]
ANEMIA: IRON DEFICIENCY	20[redacted]
CHOLELITHIASIS	20[redacted]
OTHER: DUODENITIS	20[redacted]
OTHER: INTERMITTENT BILATERAL SWELLING IN FEET	20[redacted]
OTHER: MILD AORTIOLIAC ATHEROSCLEROSIS	20[redacted]
OTHER: MILD DEGENERATIVE CHANGES THORACOLUMBAR SPINE	20[redacted]
OTHER: PERFORATED PEPTIC ULCER	20[redacted]
OTHER: RIGHT RENAL CYST	20[redacted]
OTHER: RIGHT SIDED PLEURAL EFFUSION	20[redacted]
OTHER: CLOSTRIDIUM DIFFICILE	20[redacted]
OTHER: DUODENAL EROSIONS	20[redacted]
OTHER: SPONDYLOSIS	20[redacted]

OTHER: TINY FAT CONTAINING UMBILICAL HERNIA 20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB TDM	40 MG	EOW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 63	8

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 19[redacted]
VITAMINS NOS	1 TABLET	QD	Y-M: 19[redacted]
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 19[redacted]
SULFASALAZINE	4 g (gram(s))	QD	Y-M: 19[redacted]
FISH OIL	2 TABLETS	QD	Y-M: 19[redacted]
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 19[redacted]
MESALAZINE	8 TABLETS	QD	Y-M: 19[redacted]
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -119

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 (milligram(s))	PRN	Y-M: 19[redacted]	ONGOING
VITAMINS NOS	1 TABLET	QD	Y-M: 19[redacted]	ONGOING
FISH OIL	2 TABLETS	QD	Y-M: 19[redacted]	ONGOING
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -119	ONGOING
SODIUM CHLORIDE	2 L (litre(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 56	Y-M: 20[redacted]-[redacted] / 56
METHYLPREDNISOLONE	60 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 64	Y-M: 20[redacted]-[redacted] / 67
ENOXAPARIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 65	ONGOING
MIDAZOLAM	5 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 65	Y-M: 20[redacted]-[redacted] / 65
SODIUM PHOSPHATE	266 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 65	Y-M: 20[redacted]-[redacted] / 65
FENTANYL	25 mcg (microgram(s))	PRN	Y-M: 20[redacted]-[redacted] / 65	Y-M: 20[redacted]-[redacted] / 68
OXYCODONE	5 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / 68	ONGOING
PARACETAMOL	1000 mg (milligram(s))	QID	Y-M: 20[redacted]-[redacted] / 68	ONGOING
CEFAZOLIN	1000 mg (milligram(s))	Other: TWICE	Y-M: 20[redacted]-[redacted] / 68	Y-M: 20[redacted]-[redacted] / 68
CELECOXIB	200 mg (milligram(s))	Other: TWICE	Y-M: 20[redacted]-[redacted] / 68	Y-M: 20[redacted]-[redacted] / 68
DEXAMETHASONE	4 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 68	Y-M: 20[redacted]-[redacted] / 68
DROPERIDOL	0.625 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 68	Y-M: 20[redacted]-[redacted] / 68
EPHEDRINE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 68	Y-M: 20[redacted]-[redacted] / 68
FAMOTIDINE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 68	Y-M: 20[redacted]-[redacted] / 68
GABAPENTIN	600 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 68	Y-M: 20[redacted]-[redacted] / 68
GLYCOPYRRONIUM	0.2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 68	Y-M: 20[redacted]-[redacted] / 68
KETAMINE	10 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-	Y-M: 20[redacted]-[redacted] /

			[redacted] / 68	68
KETOROLAC	30 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 68
LIDOCAINE	60 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 68
METRONIDAZOLE	500 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 68
MIDAZOLAM	2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 68
ONDANSETRON	4 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 68
PROPOFOL	150 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 68
ROCURONIUM	70 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 68
SUGAMMADEX	50 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 68
HEPARIN	5000 UNITS	TID	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 71
MAGNESIUM OXIDE	400 mg (milligram(s))	BID	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- [redacted] / 71
IBUPROFEN	600 mg (milligram(s))	Other: EVERY 6 HOURS	Y-M: 20[redacted]- [redacted] / 69	Y-M: 20[redacted]- [redacted] / 71
ENOXAPARIN	100 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 78	ONGOING
HEPARIN	25000U/250 ML UNITS	Other: AS DIRECTED	Y-M: 20[redacted]- [redacted] / 78	Y-M: 20[redacted]- [redacted] / 78
HYDROMORPHONE	0.2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 78	Y-M: 20[redacted]- [redacted] / 78
GRANISETRON	0.1 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 78	Y-M: 20[redacted]- [redacted] / 80
PROMETHAZINE	6.25 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 78	Y-M: 20[redacted]- [redacted] / 80
DEXTROSE AND SODIUM CHLORIDE INJECTION	1 L (litre(s))	Other: AS DIRECTED	Y-M: 20[redacted]- [redacted] / 78	Y-M: 20[redacted]- [redacted] / 86
KETOROLAC	15 mg (milligram(s))	Other: EVERY 6 HOURS	Y-M: 20[redacted]- [redacted] / 78	Y-M: 20[redacted]- [redacted] / 87
FLEBOBAG RING LACT	500 mL (millilitre(s))	Other: AS DIRECTED	Y-M: 20[redacted]- [redacted] / 78	Y-M: 20[redacted]- [redacted] / 90
OXYCODONE	5 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 79	ONGOING
OXYCODONE	10 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 79	Y-M: 20[redacted]- [redacted] / 85

ONDANSETRON	4 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 80	Y-M: 20[redacted]-[redacted] / 87
SODIUM CHLORIDE	1 L (litre(s))	Other: AS DIRECTED	Y-M: 20[redacted]- [redacted] / 80	Y-M: 20[redacted]-[redacted] / 87
HYOSCINE	1.5 mg (milligram(s))	Other: EVERY 3 DAYS	Y-M: 20[redacted]- [redacted] / 81	Y-M: 20[redacted]-[redacted] / 84
DROPERIDOL	0.625 mg (milligram(s))	Other: TWICE	Y-M: 20[redacted]- [redacted] / 82	Y-M: 20[redacted]-[redacted] / 82
TRAMADOL	50 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 82	Y-M: 20[redacted]-[redacted] / 88
HYDROMORPHONE	0.4 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 84	Y-M: 20[redacted]-[redacted] / 84
ONDANSETRON	4 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 84	Y-M: 20[redacted]-[redacted] / 84
SIMETICONE	160 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 84	Y-M: 20[redacted]-[redacted] / 84
LIDOCAINE	1 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 85	Y-M: 20[redacted]-[redacted] / 85
PROCHLORPERAZINE	10 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 85	Y-M: 20[redacted]-[redacted] / 87
POTASSIUM	10 mEq (milliequivalent(s))	PRN	Y-M: 20[redacted]- [redacted] / 85	Y-M: 20[redacted]-[redacted] / 89
AMIDOTRIZOIC ACID	100 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 86	Y-M: 20[redacted]-[redacted] / 86
SIMETICONE	160 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 86	Y-M: 20[redacted]-[redacted] / 86
AMINO ACIDS NOS W/CARBOHYDRATES NOS	1.5 L (litre(s))	QD	Y-M: 20[redacted]- [redacted] / 86	Y-M: 20[redacted]-[redacted] / 87
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 86	Y-M: 20[redacted]-[redacted] / 89
METOCLOPRAMIDE	10 mg (milligram(s))	QID	Y-M: 20[redacted]- [redacted] / 86	Y-M: 20[redacted]-[redacted] / 90
POTASSIUM	40 mEq (milliequivalent(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 87	Y-M: 20[redacted]-[redacted] / 87
SODIUM PHOSPHATE	15 mmol (millimole(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 88	Y-M: 20[redacted]-[redacted] / 88
DEXTROSE AND SODIUM CHLORIDE INJECTION	1 L (litre(s))	Other: AS DIRECTED	Y-M: 20[redacted]- [redacted] / 88	Y-M: 20[redacted]-[redacted] / 89
THIAMINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 88	Y-M: 20[redacted]-[redacted] / 90
METOCLOPRAMIDE	5 mg (milligram(s))	QID	Y-M: 20[redacted]- [redacted] / 90	ONGOING

TRAMADOL	50 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 90 ONGOING

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

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 64 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 87): BICARBONATE: 50 [22 - 29] NMOL/L; CHLORIDE: 80 [98 - 107] MMOL/L; PHOSPHOROUS: 2.1 [2.5 - 4.5] MG/DL; POTASSIUM: 3.1 [3.6 - 5.2] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 68): LAPAROSCOPIC SUBTOTAL COLECTOMY AND END: REMAINS HOSPITALIZED RECOVERING

AE Stopped Rx Day	71 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	DISEASE EXACERBATION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	PORTO MESENTERIC THROMBOSIS
Preferred term	門脈脾静脈腸間膜静脈血栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 77 (14 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 87): BIOCARBONATE: 50 [22 - 29] MMOL/L; CHLORIDE: 80 [98 - 107] MMOL/L; PHOSPHOROUS: 2.1 [2.5 - 4.5] MG/DL; POTASSIUM: 3.1 [3.6 - 5.2] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 77): CT ABDOMEN AND PLEVIS: DIFFUSE BOWEL DILATION DUE TO A POSSIBLE STRICTURE AT THE END ILEOSTOMY VERSUS ILEUS. PORTOMESENTERIC VENOUS THROMBOSIS.; [redacted]20[redacted] (RX DAY 85): CT OF ABDOMEN AND PELVIS: DIFFUSE SMALL BOWEL DILATATION., INCREASED IN THE DUODENUM WHICH GRADUALLY TAPERS TO NORMAL CALIBER AT THE END

ILEOSTOMY. FINDINGS ARE LIKELY RELATED TO ADYNAMIC ILEUS. NO FOCAL TRANSITION POINT. NO O; [redacted]20[redacted] (RX DAY 86): ABDOMINAL X-RAY: ORAL CONTRAST SEEN THROUGHOUT. SCATTERED LOOPS OF DISTENDED SMALL BOWEL IN THE MIDABDOMEN AND BOTH LOWER QUADRANTS. OVERALL BOWEL DISTENTION NOW BY GAS AND CONTRAST. RIGHT LOWER QUADRANT OSTOMY. NG TU

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #3: Serious Adverse Event

Event Description	SMALL BOWEL OBSTRUCTION
Preferred term	小腸閉塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 77 (14 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 87): BICARBONATE: 50 [22 - 29] MMOL/L; CHLORIDE: 80 [98 - 107] MMOL/L; PHOSPHOROUS: 2.1 [2.5 - 4.5] MG/DL; POTASSIUM: 3.1 [3.6 - 5.2] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 77): CT ABDOMEN AND PELVIS: DIFFUSE BOWEL DILATION DUE TO A POSSIBLE STRICTURE AT THE END ILEOSTOMY VERSUS ILEUS. PORTOMESENTERIC VENOUS THROMBOSIS.; [redacted]20[redacted] (RX DAY 85): CT OF ABDOMEN AND PELVIS: DIFFUSE SMALL BOWEL DILATATION, INCREASED IN THE DUODENUM WHICH GRADUALLY TAPERS TO NORMAL CALIBER AT THE END ILEOSTOMY. FINDINGS ARE LIKELY RELATED TO ADYNAMIC ILEUS. NO FOCAL TRANSITION POINT. N; [redacted]20[redacted] (RX DAY 86): ABDOMINAL X-RAY: ORAL CONTRAST SEEN THROUGHOUT. SCATTERED LOOPS OF DISTENDED SMALL BOWEL IN THE MIDABDOMEN AND BOTH LOWER QUADRANTS. OVERALL BOWEL DISTENTION, NOW BY GAS AND CONTRAST. RIGHT LOWER QUADRANT OSTOMY. NG T

AE Stopped Rx Day	90 (27 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO

SAE Criteria　HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:02:12
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の女性（米国）であり，重篤な有害事象の小腸閉塞，潰瘍性大腸炎の悪化，及び門脈腸間膜血栓症が認められた。関連する病歴は，潰瘍性大腸炎，十二指腸炎，穿孔消化性潰瘍．クロストリジウム・ディフィシレ感染，及び十二指腸びらんであった。被験者はアルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，小腸閉塞及び門脈腸間膜血栓症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，小腸閉塞は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は潰瘍性大腸炎の悪化のため病院を受診した。被験者は，頻繁な血液を伴う水様便，中等度から重度の腹痛，寝汗（非重篤），関節痛，及び疲労を訴えた。同日に被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日から [redacted] 月 [redacted] 日の間に，治療としてステロイドが静脈内投与された。被験者の大腸炎はステロイド抵抗性であると判断された。20[redacted] 年 [redacted] 月 [redacted] 日，腹腔鏡下結腸亜全摘術及び終末型回腸瘻造設が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者の容体が安定し，十分な経口摂取，排尿，及びストーマからの排泄ができる状態で退院した。疼痛は適切に管理されていた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腹痛，悪心，及びストーマ排液減少のため救急治療室を受診し，入院した。入院日に実施された腹部コンピュータ断層撮影検査の結果，門脈腸間膜静脈血栓症及び狭窄による術後イレウスが認められた。経鼻胃管が設置された。入院中，被験者は重篤な有害事象の小腸閉塞及び門脈腸間膜血栓症（20[redacted] 年 [redacted] 月 [redacted] 日発現～継続中），並びに非重篤な低リン酸血症（20[redacted] 年 [redacted] 月 [redacted] 日発現～20[redacted] 年 [redacted] 月 [redacted] 日），低カリウム血症（20[redacted] 年 [redacted] 月 [redacted] 日発現～20[redacted] 年 [redacted] 月 [redacted] 日），体液量減少（20[redacted] 年 [redacted] 月 [redacted] 日発現～20[redacted] 年 [redacted] 月 [redacted] 日），及び代謝性アルカローシス（20[redacted] 年 [redacted] 月 [redacted] 日発現～20[redacted] 年 [redacted] 月 [redacted] 日）と診断され治療が行われた。経鼻胃管が外され，食事状況は一歩前進した。被験者は門脈腸間膜血栓症のために血管内科を受診し，6 ヵ月間の外来治療の予定で抗凝固治療が開始された。薬剤が投与され，悪心及び嘔吐の治療が行われた。高カロリー輸液が実施された。リン及びカリウムが補給され，低リン酸血症（非重篤）及び低カリウム血症の治療が行われた。体液量減少に対し輸液ボーラス投与が行われた。

電解質異常の管理に関して，腎臓内科に相談し，補助を求めた。非重篤な有害事象の代謝性アルカローシス，体液量減少，低カリウム血症，及び低リン酸血症は入院中に回復した。20[redacted] 年 [redacted] 月 [redacted] 日，ストーマ周囲粘膜皮膚剥離（非重篤）が認められ，新しいストーマ装具が装着された。20[redacted] 年 [redacted] 月 [redacted] 日の退院時において，排便は良好であり，通常の食事に耐性がみられ，疼痛も適切に管理されていた。

治療薬としてデキサメタゾン，ドロペリドール，エノキサパリン，ファモチジン，ガバペンチン，グリコピロレート，ヘパリン，ケトロラク，メチルプレドニゾロン，オンダンセトロン，オキシコドン，エフェドリン，フェンタニル，イブプロフェン，ケタミン，リドカイン，酸化マグネシウム，ミダゾラム，プロポフォール，rocuronium，sodium phosphate，スガマデクス，塩化ナトリウム，ジアトリゾ酸メグルミン／ジアトリゾ酸ナトリウム，グラニセトロン，ヒドロモルフォン，乳酸リンゲル液，メトクロプラミド，パントプラゾール，塩化カリウム，プロクロルペラジン，プロメタジン，スコポラミン，シメチコン，チアミン，高カロリー輸液，トラマドール，セレコキシブ，セファゾリン，アセトアミノフェン，及びメトロニダゾールが投与された。

The patient's past medications include:

AZULFIDINE for ULCERATIVE COLITIS (19[redacted] - 19[redacted])

PREDNISONE for ULCERATIVE COLITIS (19[redacted] - 19[redacted])

ASCOLIN for ULCERATIVE COLITIS (19[redacted] - 19[redacted])

PENTASA for ULCERATIVE COLITIS (19[redacted] - 19[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Small bowel obstruction (10041055) (Small intestinal obstruction (10041101)) [v.20.1] [10041055]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

3) Portosplenomesenteric venous thrombosis (10077623) (Portosplenomesenteric venous thrombosis (10077623)) [v.20.1] [10077623]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of SMALL BOWEL OBSTRUCTION

- Investigator: Ulcerative colitis.

- AbbVie: Event more likely a complication of recent abdominal surgical procedure. Additional risk factors include history of pre-existing ulcerative colitis, duodenitis, duodenal erosions, and perforated peptic ulcer.

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Disease exacerbation

- AbbVie: Event more likely related to pre existing ulcerative colitis

Event of PORTO MESENTERIC THROMBOSIS

- Investigator: Ulcerative Colitis

- AbbVie: Event is more likely related to colectomy that was performed 10 days prior to the onset of the event. Subject's pre-existing ulcerative colitis increased the risk of the thromboembolic complication.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL CT: Diffuse bowel dilation due to a possible stricture at the end ileostomy versus ileus, portomesenteric venous thrombosis

[redacted] 20[redacted] ABDOMINAL CT: 1. Diffuse small bowel dilatation, increased in the duodenum which gradually tapers to normal caliber at the end ileostomy. Findings are likely related to adynamic ileus. No focal transition point. No organized or drainable fluid collection. 2. Stable appearing right posterior portal vein thrombus.

[redacted] 20[redacted] ABDOMINAL X-RAY: Compared to [redacted] 20[redacted]: Oral contrast seen throughout scattered loops of distended small bowel in the midabdomen and both lower quadrants. Overall bowel distention,

now by gas and contrast, is not significantly changed compared to prior. Right lower quadrant ostomy. NG tube with tip and sidehole in the gastric fundus. Residual excreted contrast in the bladder.

[redacted] 20[redacted] ANION GAP: 18 no unit (normal 7 to 15)

[redacted] 20[redacted] ANION GAP: 4 no unit (normal 7 to 15)

[redacted] 20[redacted] ANION GAP: 10 no unit (normal 7 to 15)

[redacted] 20[redacted] BICARBONATE: 38 MMOL/L (normal 22 to 29)

[redacted] 20[redacted] BICARBONATE: 50 MMOL/L (normal 22 to 29)

[redacted] 20[redacted] BICARBONATE: 28 MMOL/L (normal 22 to 29)

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

[redacted] 20[redacted] BODY TEMPERATURE: 36 Degrees C

[redacted] 20[redacted] C. DIFFICILE TOXIN: NEGATIVE

[redacted] 20[redacted] CALCIUM: 4.03 mg/dL (normal 4.65 to 5.3)

[redacted] 20[redacted] CHLORIDE: 82 MMOL/L (normal 98 to 107)

[redacted] 20[redacted] CHLORIDE: 80 MMOL/L (normal 98 to 107)

[redacted] 20[redacted] CHLORIDE: 101 MMOL/L (normal 98 to 107)

[redacted] 20[redacted] CREATININE: 0.7 mg/dL (normal 0.6 to 1.1)

[redacted] 20[redacted] CREATININE: 0.6 mg/dL (normal 0.6 to 1.1)

[redacted] 20[redacted] EGFR: . >60 mL/min/BSA

[redacted] 20[redacted] ERYTHROCYTES: 3.62 X10**12/L (normal 3.9 to 5.03)

[redacted] 20[redacted] ERYTHROCYTES: 3.25 X10**12/L (normal 3.9 to 5.03)

[redacted] 20[redacted] HCO3: 44 MMOL/L (normal 22 to 26)

[redacted] 20[redacted] HEART RATE: 65 bpm

[redacted] 20[redacted] HEMATOCRIT: 32.3 % (normal 34.9 to 44.5)

[redacted] 20[redacted] HEMATOCRIT: 31.0 % (normal 34.9 to 44.5)

[redacted] 20[redacted] HEMOGLOBIN: 10.5 G/DL (normal 12.0 to 15.5)

[redacted] 20[redacted] HEMOGLOBIN: 9.3 G/DL (normal 12.0 to 15.5)

[redacted] 20[redacted] HEMOGLOBIN: 9.7 G/DL (normal 12.0 to 15.5)

[redacted] 20[redacted] LEUKOCYTES: 7.1 X10**9/L (normal 3.5 to 10.5)

[redacted] 20[redacted] LEUKOCYTES: 13.5 X10**9/L (normal 3.5 to 10.5)

[redacted] 20[redacted] PCO2: 50 mm Hg (normal 35 to 45)

[redacted] 20[redacted] PH: 7.55 no unit (normal 7.35 to 7.45)

[redacted] 20[redacted] PHOSPHOROUS: 2.1 mg/dL (normal 2.5 to 4.5)

[redacted] 20[redacted] PHOSPHOROUS: 2.9 mg/dL (normal 2.5 to 4.5)

[redacted] 20[redacted] PLATELETS: 685 X10**9/L (normal 150 to 450)

[redacted] 20[redacted] PLATELETS: 642 X10**9/L (normal 150 to 450)

[redacted] 20[redacted] POTASSIUM: 3.1 MMOL/L (normal 3.6 to 5.2)

[redacted] 20[redacted] POTASSIUM: 3.9 MMOL/L (normal 3.6 to 5.2)

[redacted] 20[redacted] SODIUM: 134 MMOL/L (normal 135 to 145)

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

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
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	MALE	White

Medical History	Onset Year
OTHER: ATTENTION DEFICIT DISORDER	20[redacted]
OTHER: HIP DYSPLASIA	20[redacted]
OTHER: ACNE	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 253	196

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
OBETROL	10 mg (milligram(s))	QD	Y-M: 20[redacted]
VITAMINS NOS	1 TABLET	QD	Y-M: 20[redacted]
MULTIVITAMINS, OTHER COMBINATIONS	1 TABLET	PRN	Y-M: 20[redacted]
MESALAZINE	2.4 mg (milligram(s))	BID	Y-M: 20[redacted]
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -229
TRITICUM AESTIVUM	1 TABLET	PRN	Y-M: 20[redacted] / -229
SUPREP BOWEL PREP	12 OUNCES	Other: DIVIDED DOSES	Y-M: 20[redacted] / -14
PROPOFOL	350 mg (milligram(s))	Other: DIVIDED DOSING	Y-M: 20[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
OBETROL	10 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
VITAMINS NOS	1 TABLET	QD	Y-M: 20[redacted]	ONGOING
MULTIVITAMINS, OTHER COMBINATIONS	1 TABLET	PRN	Y-M: 20[redacted]	ONGOING
TRITICUM AESTIVUM	1 TABLET	PRN	Y-M: 20[redacted] / -229	ONGOING
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / / 207	Y-M: 20[redacted] / 221
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / / 222	Y-M: 20[redacted] / 245
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / 242	ONGOING
HYOSCYAMINE	0.375 mg (milligram(s))	PRN	Y-M: 20[redacted] / 247	ONGOING
PROPOFOL	420 mg (milligram(s))	Other: DIVIDED DOSES	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 268
AZATHIOPRINE	50 mg (milligram(s))	TID	Y-M: 20[redacted] / 261	Y-M: 20[redacted] / 294
GOLIMUMAB	200 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 263	Y-M: 20[redacted] / 263
GOLIMUMAB	100 mg (milligram(s))	Other: EVERY FOUR	Y-M: 20[redacted]	ONGOING

		WEEKS	/ 277
HYDROCORTISONE	1 SUPPOSITORY	Other: AT BEDTIME	Y-M: 20[redacted] ONGOING / 280
MESALAZINE	2.4 g (gram(s))	BID	Y-M: 20[redacted] ONGOING / 280
METHYLPREDNISOLONE	NOT REPORTED	Other: CONTINUOUS	Y-M: 20[redacted] ONGOING / 280
OXYCOCET	1 TABLET	PRN	Y-M: 20[redacted] ONGOING / 281
IOPAMIDOL	100 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted] Y-M: 20[redacted] / / 283 283
FENTANYL	100 mcg (microgram(s))	Other: DIVIDED DOSES	Y-M: 20[redacted] Y-M: 20[redacted] / / 289 289
MIDAZOLAM	5 mg (milligram(s))	Other: DIVIDED DOSES	Y-M: 20[redacted] Y-M: 20[redacted] / / 289 289
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] ONGOING / 295
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] ONGOING / 295

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 245
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	349 (96 DAYS AFTER LAST TREATMENT)
Duration of AE	105 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HISTORY OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（米国）であり，重篤な有害事象の潰瘍性大腸炎の増悪が認められた。関連する病歴は，左側潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は，連日の下痢，血便，腹部痙攣，失禁，及び関節痛を訴えた。被験者は，日常生活を送ることが困難であると診断された後に入院した。入院中に軟性 S 状結腸鏡検査及び生検が実施された。外科に相談を行った結果，外科手術を実施する前に他の投薬治療を試みるよう助言された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月，潰瘍性大腸炎の増悪は回復した。
治療薬として Percocet，prednisone，アザチオプリン，Lialda（メサラジン），Cortifoam（ヒドロコルチゾン酢酸エステル），及び Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム）が投与された。

The patient's past medications include:

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METRONIDAZOLE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: History of ulcerative colitis.

- AbbVie: The event is exacerbation of underlying UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Flexible sigmoidoscopy:

The patient's results were: rectum 2 = Moderate disease (marked erythema, absent vascular2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions); sigmoid 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions); descending colon 0 = Normal or inactive disease; and transverse colon 0 = Normal or inactive disease. There was a presence of friability and the subscore was 2.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: AMOXICILLIN ALLERGY	19[redacted]
OTHER: NEEDLE PHOBIA	19[redacted]
SURGERY: RIGHT KNEE ACL SURGERY	19[redacted]
OTHER: OCCASIONAL ABDOMINAL PAIN	20[redacted]
OTHER: OCCASIONAL DIARRHEA	20[redacted]
OTHER: OCCASIONAL RECTAL BLEEDING	20[redacted]
OTHER: INTERNAL HEMORRHOIDS	20[redacted]
MIGRAINE HEADACHE	20[redacted]
SURGERY: BUNION RIGHT FOOT SURGERY	20[redacted]
OTHER: HERNIATED DISCS LOWER BACK	20[redacted]
DIVERTICULITIS: RIGHT SIDED	20[redacted]
OTHER: FOLLICLE RIGHT OVARY	20[redacted]
OTHER: PANDIVERTICULOSIS	20[redacted]
OTHER: TINY CYST RIGHT LOBE LIVER	20[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
OTHER: IRRITABLE BOWEL SYNDROME	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	8	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 59	[redacted]20[redacted] / 358	300

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ASCORBIC ACID	1 TABLET	PRN	Y-M: 20[redacted]
ANOVLAR	1 TABLET	QD	Y-M: 20[redacted]
LORATADINE	1 TABLET	PRN	Y-M: 20[redacted]
MESALAZINE	3.6 g (gram(s))	QD	Y-M: 20[redacted]
HYOSCYAMINE	0.375 mg (milligram(s))	PRN	Y-M: 20[redacted] / -201
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -88
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -61
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -31
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -24
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -17
BISACODYL	2 TABLETS	Other: ONCE	Y-M: 20[redacted] / -8
MACROGOL 3350	255 g (gram(s))	Other: DIVIDED DOSES	Y-M: 20[redacted] / -8
PROPOFOL	350 mg (milligram(s))	Other: DIVIDED DOSES	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
ASCORBIC ACID	1 TABLET	PRN	Y-M: 20[redacted]	ONGOING
ANOVLAR	1 TABLET	QD	Y-M: 20[redacted]	ONGOING
LORATADINE	1 TABLET	PRN	Y-M: 20[redacted]	ONGOING
MESALAZINE	3.6 g (gram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 223
HYDROCORTISONE	1 APPLICATION	PRN	Y-M: 20[redacted] / 23	ONGOING
DIPHENHYDRAMINE	50 mg (milligram(s))	PRN	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 269
HYOSCYAMINE	0.125 mg (milligram(s))	PRN	Y-M: 20[redacted] / 92	ONGOING
IOPAMIDOL	100 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 241
CIPROFLOXACIN	400 mg (milligram(s))	BID	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 243
DIPHENHYDRAMINE	25 mg (milligram(s))	PRN	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 243
HYDROCORTISONE	50 mg (milligram(s))	TID	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 243
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 243
MORPHINE	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 243
ONDANSETRON	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 243
POTASSIUM	UNKNOWN mL (millilitre(s))	PRN	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 243
SODIUM CHLORIDE	1000 mL (millilitre(s))	PRN	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 243
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 252

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 241
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 241): CT ABDOMEN AND PELVIS WITH IV CONTRAST: SIGMOID COLITIS AND PROCTITIS WITH PROMINENT ADJUACENT LYMPH NODES. THE PATIENT DOES HAVE MODERATE COLONIC DIVERTICULUM AND DISTAL SIGMOID DIVERTICULITIS IS NOT FULLY EXCLUDED. NO ABSCESS FORMATION.

AE Stopped Rx Day	252
Duration of AE	12 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HISTORY OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（米国）であり，重篤な有害事象の潰瘍性大腸炎再燃が認められた。関連する病歴は，不定期な下痢，不定期な直腸出血，内痔核，片頭痛，全大腸憩室症，右側大腸憩室症，季節性アレルギー，左側潰瘍性大腸炎，過敏性腸症候群であった。被験者は元喫煙者（1 日当たり 0.5 箱，喫煙期間 8 年）であり，アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃は回復した。

本事象の発現前には，20[redacted] 年 [redacted] 月以降（潰瘍性大腸炎の診断以降）定期的な再燃が認められている。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は，血便，腹痛，及び悪心を訴えた。臨床検査値及び便がモニタリングされた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてモルヒネ，Flagyl（メトロニダゾール），塩化カリウム，ヒドロコルチゾン，prednisone，Zofran（オンダンセトロン塩酸塩水和物），及び Cipro（シプロフロキサシン）が投与された。

The patient's past medications include:

HYOSCYAMINE for IRRITABLE BOWEL SYNDROME ([redacted] 20[redacted] - 19 [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

---

1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.22.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ULCERATIVE COLITIS FLARE

- Investigator: History of ulcerative colitis

- AbbVie: .Event more likely related to ulcerative colitis flare from pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CT ABDOMEN AND PELVIS WITH IV CONTRAST: SIGMOID COLITIS AND PROCTITIS WITH PROMINENT ADJUACENT LYMPH NODES. THE PATIENT DOES HAVE MODERATE COLONIC DIVERTICULUM AND DISTAL SIGMOID DIVERTICULITIS IS NOT FULLY EXCLUDED. NO ABSCESS FORMATION.

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
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	5[redacted]	MALE	Asian

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 121	64

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1600 mg (milligram(s))	QD	Y-M: 20[redacted] / -101
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -101
BISACODYL	5 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -3
MACROGOL 3350	240 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted] / -3
MAGNESIUM CITRATE	284 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted] / -3
LIDOCAINE	40 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -2
PROPOFOL	280 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -2

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1600 mg (milligram(s))	QD	Y-M: 20[redacted] / -101	ONGOING
RANITIDINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / 6	ONGOING
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 74
LIDOCAINE	40 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 58
PROPOFOL	180 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 58
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 75	ONGOING
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / 75	Y-M: 20[redacted] / 77
MESALAZINE	4 g (gram(s))	PRN	Y-M: 20[redacted] / 75	Y-M: 20[redacted] / 77
OXYCOCET	5/325 mg (milligram(s))	PRN	Y-M: 20[redacted] / 75	Y-M: 20[redacted] / 77
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 75	Y-M: 20[redacted] / 79
MESALAZINE	800 mg (milligram(s))	TID	Y-M: 20[redacted] / 75	Y-M: 20[redacted] / 79
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 75	Y-M: 20[redacted] / 84

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 75
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 75): HEMATOCRIT: 0.28 [0.39 - 0.5] FRACTION

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 76): CT OF ABD: RECTOSIGMOID COLITIS. THE RECTUM AND SIGMOID ARE FEATURELESS. THIS FINDING CAN BE SEEN IN ULCERATIVE COLITIS AS WELL AS REPEAT EPISODES OF COLITIS.

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	INCREASED BLEEDING POSSIBLY RELATED TO RECENT COLONOSCOPY WITH MULTIPLE BIOPSIES.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（米国）であり，重篤な有害事象の潰瘍性大腸炎再燃が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者から，前日より血便のエピソードが 2 回発現したとの報告があった。また，下腹部の痙攣のうち左下腹部がさらに悪いとの報告もあった。さらに，被験者は悪寒を訴えたが，悪心・嘔吐及び発熱はなかった。救急外来のトリアージ記録には，被験者が数日間にわたる断続的な浮動性めまいを訴えていたとの報告があった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，腹痛はなく，排便の頻度及び便中の出血量は減少していた。

治療薬としてメサラジン，Flagyl（メトロニダゾール），prednisone，Asacol（メサラジン），ロペラミド，sodium ferric gluconate，Percocet，及び Cipro（シプロフロキサシン）が投与された。

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ULCERATIVE COLITIS FLARE

- Investigator: Increased bleeding possibly related to recent colonoscopy with multiple biopsies.

- AbbVie: There is limited information, but the symptoms relate to worsenng of ulcerative colitis. More details needed.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] colonoscopy:

Rectum: severe disease(spontaneous bleeding, ulceration)

Sigmoid: severe disease(spontaneous bleeding, ulceration)

Descending colon : normal or inactive disease

Transverse colon: normal or inactive disease

Ascending colon/cecum: normal or inactive disease

[redacted] 20[redacted] CT of abdomen:

Rectosigmoid colitis. The rectum and sigmoid are featureless. This finding can be seen in ulcerative colitis as well as repeat episodes of colitis.

[redacted] 20[redacted] hematocrit: 28.4

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
双極性障害	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	FEMALE	Black

Medical History	Onset Year
DEPRESSION: DEPRESSION	19[redacted]
OTHER: PENICILLIN ALLERGY	19[redacted]
OTHER: POST TRAUMATIC STRESS DISORDER	19[redacted]
OTHER: TEGRETOL ALLERGY	19[redacted]
SEIZURE DISORDER/CONVULSIONS: PARTIAL SEIZURE DISORDER	19[redacted]
ASTHMA: ASTHMA (MILD)	19[redacted]
GASTROINTESTINAL BLEED: RECTAL BLEEDING	19[redacted]
OTHER: ABDOMINAL BLOATING	19[redacted]
OTHER: ABDOMINAL GAS	19[redacted]
OTHER: ABDOMINAL PAIN	19[redacted]
OTHER: ANXIETY	19[redacted]
OTHER: CONSTIPATION	19[redacted]
OTHER: DIARRHEA	19[redacted]
OTHER: FATIGUE	19[redacted]
OTHER: FECAL INCONTINENCE	19[redacted]
OTHER: GERD	19[redacted]
OTHER: HEMATOCHEZIA	19[redacted]
OTHER: HEMORRHOIDS	19[redacted]
OTHER: INDIGESTION	19[redacted]
OTHER: NAUSEA	19[redacted]
OTHER: PANIC ATTACKS	19[redacted]
OTHER: RECTAL PAIN	19[redacted]
OTHER: VOMITING	19[redacted]
ANEMIA: NA	19[redacted]
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	19[redacted]

MIGRAINE HEADACHE: MIGRAINE HEADACHES	19[redacted]
OTHER: BIPOLAR DISORDER	20[redacted]
OTHER: BACK PAIN	20[redacted]
OTHER: SCOLIOSIS	20[redacted]
OTHER: CHEST PAIN	20[redacted]
OTHER: IRREGULAR HEARTBEAT	20[redacted]
SURGERY: COLONOSCOPY	20[redacted]
SURGERY: EGD	20[redacted]
OTHER: REMICADE ALLERGY	20[redacted]
SURGERY: COLONOSCOPY	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: SUICIDE ATTEMPT	20[redacted]
SURGERY: COLONOSCOPY	20[redacted]
OTHER: GRANULOMAS (RIGHT LOWER LUNG)	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 358	303

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BALSALAZIDE	9 g (gram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
SALBUTAMOL	2 PUFFS	PRN	Y-M: 20[redacted]
VENLAFAXINE	75 mg (milligram(s))	BID	Y-M: 20[redacted]
QUETIAPINE	75 mg (milligram(s))	Other: QAM	Y-M: 20[redacted]-[redacted] / -228
OMEPRAZOLE	20 mg (milligram(s))	Other: QAM	Y-M: 20[redacted]-[redacted] / -138
VALPROIC ACID	750 mg (milligram(s))	Other: QPM	Y-M: 20[redacted]-[redacted] / -138
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -33
DRUGS FOR CONSTIPATION	1 PACK	Other: ONCE	Y-M: 20[redacted]-[redacted] / -16
DRUGS FOR CONSTIPATION	1 PACK	Other: ONCE	Y-M: 20[redacted]-[redacted] / -9
PROPOFOL	200 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[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
BALSALAZIDE	9 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
SALBUTAMOL	2 PUFFS	PRN	Y-M: 20[redacted]	ONGOING
VENLAFAXINE	75 mg (milligram(s))	BID	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 216
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -33	ONGOING
LURASIDONE	80 mg (milligram(s))	Other: QPM	Y-M: 20[redacted]-[redacted] / 164	Y-M: 20[redacted]-[redacted] / 194
METFORMIN	500 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 169	ONGOING
CLONAZEPAM	0.5 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 195	ONGOING
LURASIDONE	60 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 195	Y-M: 20[redacted]-[redacted] / 208

Event #1: Serious Adverse Event

Event Description	WORSENING OF BIPOLAR DISORDER
Preferred term	双極性障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 207
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	

AE Stopped Rx Day	208
Duration of AE	2 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HISTORY OF BIPOLAR WITH SUICIDAL IDEATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（米国）であり，重篤な有害事象の双極性障害の悪化が認められた。関連する病歴は，うつ病，不安，双極性障害，及び自殺企図であった。

20[redacted] 年 [redacted] 月 [redacted] 日，双極性障害の悪化が認められた。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日～20[redacted] 年 [redacted] 月 [redacted] 日に，双極性障害の悪化及び自殺念慮のため入院した。双極性障害の悪化及び自殺念慮の兆候及び症状が認められた。心理カウンセリングセッションの実施及び投薬変更の臨床経過を経て，20[redacted] 年 [redacted] 月 [redacted] 日に双極性障害の悪化は回復した。

治療薬として Effexor（ベンラファキシン塩酸塩），ルラシドン，及び levomilnacipran が投与された。

The patient's past medications include:

DEPAKOTE ER for BIPOLAR DISORDER ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

OMEPRAZOLE for GERD ([redacted] 20[redacted] - [redacted] 20[redacted])

PROPOFOL for COLONOSCOPY and SEDATION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

AZITHROMYCIN DIHYDRATE for RIGHT EAR INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PERCOCET for RIGHT EAR PAIN ([redacted] 20[redacted] - [redacted] 20[redacted])

PENICILLIN for UNKNOWN INDICATION

REMICADE for UNKNOWN INDICATION

TEGRETOL for UNKNOWN INDICATION

Causality for HUMIRA (Open Label)

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1) Bipolar affective disorder aggravated (10004910) (Bipolar disorder (10057667)) [v.19.0] [10004910]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF BIPOLAR DISORDER

- Investigator: History of bipolar with suicidal ideation.

- AbbVie: Past history of bipolar disease and the patient is not on stable and long term use of bipolar disease medications recently.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] COlonoscopy:

Rectum 3 = severe disease (spontaneous bleeding, ulceration).

Sigmoid 1 = mild disease (erythema, decreased vascular pattern, mild friability)

Descending colon 0 = Normal or inactive disease

Transverse colon 0 = Normal or inactive disease

Ascending colon/cecum 0 = Normal or inactive disease

Presence of friability yes

Subscore 3

[redacted] 20[redacted] Colonoscopy:

Rectum 1 = mild disease (erythema, decreased vascular pattern, mild friability)

Sigmoid 1 = mild disease (erythema, decreased vascular pattern, mild friability)

Descending colon 1 = mild disease (erythema, decreased vascular pattern, mild friability)

Transverse colon 0 = Normal or inactive disease

Ascending colon/cecum 0 = Normal or inactive disease

Presence of friability no

Subscore 1

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
急性膵炎	X			
クロストリジウム・ディフィシレ感染	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	MALE	White

Medical History	Onset Year
OTHER: ALLERGY TO PENICILLIN	19[redacted]
OTHER: ALLERGY TO CATS	20[redacted]
OTHER: ABDOMINAL BLOATING	20[redacted]
OTHER: ABDOMINAL PAIN	20[redacted]
OTHER: DIARRHEA	20[redacted]
OTHER: INTERMITTENT BACK PAIN (ENTIRE)	20[redacted]
OTHER: INTERMITTENT FATIGUE	20[redacted]
OTHER: INTERMITTENT INSOMNIA	20[redacted]
OTHER: INTERMITTENT WEIGHT LOSS	20[redacted]
OTHER: RECTAL BLEEDING	20[redacted]
SURGERY: COLONOSCOPY	20[redacted]
SURGERY: COLONOSCOPY	20[redacted]
KIDNEY DISORDER: KIDNEY STONES (RIGHT SIDED)	20[redacted]
OTHER: INTERMITTENT HEMATURIA (SECONDARY TO KIDNEY STONES)	20[redacted]
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
OTHER: INTOLERANCE TO ORAL IRON SUPPLEMENTATION	20[redacted]
HYPERTENSION	20[redacted]
OTHER: ORAL CANDIDIASIS	20[redacted]
SURGERY: COLONOSCOPY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	CURRENT			
CIGARETTES	CURRENT	0.5 PACKS	19	
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 60	[redacted]20[redacted] / 331	272

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted]
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -53
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -53
PREDNISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -53
MESALAZINE	7.2 g (gram(s))	QD	Y-M: 20[redacted] / -48
MILK SUBSTITUTES	16 OZ	QD	Y-M: 20[redacted] / -48
PREDNISONE	60 mg (milligram(s))	QD	Y-M: 20[redacted] / -48
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -34
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -27
FLUCONAZOLE	200 mg (milligram(s))	QD	Y-M: 20[redacted] / -20
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -20
FLUCONAZOLE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -19
SUPREP BOWEL PREP	8 OZ	QD	Y-M: 20[redacted] / -14
PROPOFOL	220 mg (milligram(s))	Other: ONCE	Y-M: 20[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
MESALAZINE	7.2 g (gram(s))	QD	Y-M: 20[redacted] / 48	ONGOING
MILK SUBSTITUTES	16 OZ	QD	Y-M: 20[redacted] / 48	ONGOING
LISINOPRIL	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 193	ONGOING
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 200	ONGOING
HYDROCHLOROTHIAZIDE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 345
MUPIROCIN	1 APPLICATION	BID	Y-M: 20[redacted] / 318	Y-M: 20[redacted] / 374

Event #1: Serious Adverse Event

Event Description	ACUTE PANCREATITIS
Preferred term	急性膵炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 345 (14 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	360 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	16 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	CLOSTRIDIUM DIFFICILE INFECTION
Preferred term	クロストリジウム・ディフィシレ感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 348 (17 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	360 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	13 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（米国）であり，重篤な有害事象の急性膵炎が認められた。関連する病歴は，腹部膨満，腹痛，下痢，断続的な体重減少，及び潰瘍性大腸炎であった。
20[redacted] 年[redacted] 月[redacted] 日，急性膵炎が認められた。20[redacted] 年[redacted] 月[redacted] 日，急性膵炎は回復した。
20[redacted] 年[redacted] 月[redacted] 日，被験者は重度の上腹部痛のため入院した。暫定的診断結果は急性膵炎と一致していた。
治療として抗生剤が投与され，酵素補充療法及び一酸化窒素吸入療法が実施された。
また，被験者は 1 日当たり 16 オンスのケフィア（栄養補助食品）を併用して経口摂取した（20[redacted] 年[redacted] 月[redacted] 日～継続中）。

The patient's past medications include:

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

MUPIROCIN for RASH ([redacted] 20[redacted] - [redacted] 20[redacted])

PENICILLIN for UNKNOWN INDICATION

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Acute pancreatitis (10000971) (Pancreatitis acute (10033647)) [v.19.1] [10000971]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of ACUTE PANCREATITIS

- Investigator: N/A

- AbbVie: THE PATIENT HAS KNOWN MEDICAL HISTORY OF SYMPTOMATIC/TREATED ABDOMINAL PAIN SINCE 20[redacted].

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（米国）であり，重篤な有害事象のクロストリジウム・ディフィシレ感染が認められた。関連する病歴は，下痢，直腸出血，及び潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，クロストリジウム・ディフィシレ感染が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性膵炎のため入院し，数日後にクロストリジウム・ディフィシレ感染と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，クロストリジウム・ディフィシレ感染は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

PENICILLIN for UNKNOWN INDICATION

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Clostridium difficile infection (10054236) (Clostridium difficile infection (10054236)) [v.19.0] [10054236]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of CLOSTRIDIUM DIFFICILE INFECTION

- Investigator: Unknown

- AbbVie: Related to underlying UC

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: SEASONAL ALLERGIES	19[redacted]
SURGERY: BENIGN RIGHT BREAST LUMPECTOMY	19[redacted]
MIGRAINE HEADACHE	20[redacted]
OTHER: ANAL FISSURES	20[redacted]
OTHER: CHRONIC VAGINAL YEAST INFECTIONS	20[redacted]
OTHER: APPENDICITIS	20[redacted]
OTHER: HAIR LOSS	20[redacted]
SURGERY: BENIGN CERVICAL POLYP REMOVAL	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	1	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 121	66

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
RIBOFLAVIN	400 mg (milligram(s))	QD	Y-M: 20[redacted]
ALOE VERA	3 CAPFULS	QD	Y-M: 20[redacted]
CALCIUM	1 CAPSULE	QD	Y-M: 20[redacted]
PROBIOTICS NOS	1-2 PACKETS	QD	Y-M: 20[redacted]
BIOTIN	1 CAPSULE	QD	Y-M: 20[redacted] / -138
ZINGIBER OFFICINALE	1 CAPSULE	QD	Y-M: 20[redacted] / -138
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -32
BISACODYL	10 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -8
MACROGOL 3350	238 g (gram(s))	Other: ONCE	Y-M: 20[redacted] / -8
PHENYLEPHRINE	100 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / -7
PROPOFOL	620 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -7
SODIUM CHLORIDE	200 mL (millilitre(s))	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
RIBOFLAVIN	400 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
ALOE VERA	3 CAPFULS	QD	Y-M: 20[redacted]	ONGOING
CALCIUM	1 CAPSULE	QD	Y-M: 20[redacted]	ONGOING
PROBIOTICS NOS	1-2 PACKETS	QD	Y-M: 20[redacted]	ONGOING
BIOTIN	1 CAPSULE	QD	Y-M: 20[redacted] / -138	ONGOING
ZINGIBER OFFICINALE	1 CAPSULE	QD	Y-M: 20[redacted] / -138	ONGOING
METHYLPREDNISOLONE	20 mg (milligram(s))	Other: Q8H	Y-M: 20[redacted] / 126	Y-M: 20[redacted] / 128
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] /	ONGOING

128

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

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 116
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	129 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	DISEASE UNDER STUDY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（米国）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（左側）及び裂肛であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，持続性直腸炎の症状が認められ，被験者は入院した。下痢及び直腸出血を含む兆候及び症状が認められた。排便回数は 1 日当たり 6～7 回で毎回血便であったが，時折血液／粘液のみであった。被験者は便意切迫，不定期な失禁，排便時の直腸痛，及び心窩部痛を

訴えた。不定期な悪心が認められたが，嘔吐はみられなかった。経口による食事に耐性が認められた。被験者は疲労を訴え，微熱が 2 日間続いたが回復した。
治療薬として Prilosec，Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム），prednisone，及び Entyvio（ベドリズマブ）が投与された。

The patient's past medications include:

FLAGYL for IBD (20[redacted] - 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Disease under study

- AbbVie: The event is exacerbation of the underlying disease of ulcerative colitis.

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
潰瘍性大腸炎	X	X		
脱水	X	X		
低ナトリウム血症	X			
鉄欠乏性貧血	X			
血小板増加症	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	6[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: APPENDECTOMY	19[redacted]
OTHER: INTERNAL HEMORRHOIDS	19[redacted]
ARTHRALGIA: PERIPHERAL ARTHRALGIAS	19[redacted]
OTHER: VON WILLEBRAND'S	19[redacted]
OTHER: ALLERGIC TO ASPIRIN	20[redacted]
ASTHMA	20[redacted]
GASTROINTESTINAL BLEED: RECTAL BLEED	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: CLOSTRIDIUM DIFFICILE	20[redacted]
OTHER: HERPES ZOSTER (SHINGLES)	20[redacted]
OTHER: TORN RIGHT ROTATOR CUFF	20[redacted]
OSTEOPOROSIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	5	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 127	71

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CALCIUM CARBONATE	500 mg (milligram(s))	PRN	Y-M: 19[redacted]
ZOLPIDEM	5 mg (milligram(s))	PRN	Y-M: 19[redacted]
PARACETAMOL	450 mg (milligram(s))	PRN	Y-M: 20[redacted]
SERETIDE	100/50 INHALATION	BID	Y-M: 20[redacted]
MESALAZINE	4.8 mg (milligram(s))	BID	Y-M: 20[redacted]
CALCIUM CARBONATE	500 mg (milligram(s))	QD	Y-M: 20[redacted] / -101
COLECALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted] / -101
VITAMIN B12 NOS	1000 mcg (microgram(s))	QD	Y-M: 20[redacted] / -101
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -49
SUPREP BOWEL PREP	ONE PACKAGE	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
CALCIUM CARBONATE	500 mg (milligram(s))	PRN	Y-M: 19[redacted]	ONGOING
ZOLPIDEM	5 mg (milligram(s))	PRN	Y-M: 19[redacted]	ONGOING
PARACETAMOL	450 mg (milligram(s))	PRN	Y-M: 20[redacted]	ONGOING
SERETIDE	100/50 INHALATION	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 129
MESALAZINE	4.8 mg (milligram(s))	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 148

CALCIUM CARBONATE	500 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / -101	ONGOING
COLECALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted]- [redacted] / -101	ONGOING
VITAMIN B12 NOS	1000 mcg (microgram(s))	QD	Y-M: 20[redacted]- [redacted] / -101	ONGOING
PREPARATION H	ONE APPLICATION TOPICAL	PRN	Y-M: 20[redacted]- [redacted] / 71	Y-M: 20[redacted]- [redacted] / 186
ACICLOVIR	800 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 98	Y-M: 20[redacted]- [redacted] / 104
OSELTAMIVIR	75 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 102	Y-M: 20[redacted]- [redacted] / 107
SALBUTAMOL	2 PUFFS	PRN	Y-M: 20[redacted]- [redacted] / 102	Y-M: 20[redacted]- [redacted] / 186
CEFDINIR	300 mg (milligram(s))	BID	Y-M: 20[redacted]- [redacted] / 103	Y-M: 20[redacted]- [redacted] / 104
ESCITALOPRAM	10 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 115	Y-M: 20[redacted]- [redacted] / 186
ONDANSETRON	4 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 129	Y-M: 20[redacted]- [redacted] / 132
METHYLPREDNISOLONE	40 mg (milligram(s))	Other: EVERY 6 HOURS	Y-M: 20[redacted]- [redacted] / 129	Y-M: 20[redacted]- [redacted] / 133
MORPHINE	2 mg (milligram(s))	Other: EVERY 3 HOURS PRN	Y-M: 20[redacted]- [redacted] / 130	Y-M: 20[redacted]- [redacted] / 130
ACICLOVIR	800 mg (milligram(s))	Other: FIVE TIMES DAILY FOR 10 DAYS	Y-M: 20[redacted]- [redacted] / 131	Y-M: 20[redacted]- [redacted] / 140
HYDROCORTISONE	ONE APPLICATION RECTALLY	BID	Y-M: 20[redacted]- [redacted] / 132	ONGOING
HYDROMORPHONE	0.5 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 132	Y-M: 20[redacted]- [redacted] / 134
PANTOPRAZOLE	40 mg (milligram(s))	Other: EVERY 12 HOURS	Y-M: 20[redacted]- [redacted] / 132	Y-M: 20[redacted]- [redacted] / 135
SERETIDE	ONE INHALATION	BID	Y-M: 20[redacted]- [redacted] / 132	Y-M: 20[redacted]- [redacted] / 186
HYDRALAZINE	10 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 133	Y-M: 20[redacted]- [redacted] / 133
POTASSIUM	60 mEq (milliequivalent(s))	Other: ONCE	Y-M: 20[redacted]- [redacted] / 134	Y-M: 20[redacted]- [redacted] / 134
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 134	Y-M: 20[redacted]- [redacted] / 161
AMLODIPINE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 135	Y-M: 20[redacted]- [redacted] / 148

PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 136	Y-M: 20[redacted]- / 161
ORABASE	ONE TOPICAL APPLICATION	PRN	Y-M: 20[redacted]- [redacted] / 148	Y-M: 20[redacted]- / 186
RED BLOOD CELLS	2 UNITS PACKED RED BLOOD CELLS 2 UNITS	Other: ONCE	Y-M: 20[redacted]- [redacted] / 162	Y-M: 20[redacted]- / 162
HYDROMORPHONE	0.5 mg (milligram(s))	Other: EVERY THREE HOURS PRN	Y-M: 20[redacted]- [redacted] / 162	Y-M: 20[redacted]- / 164
METHYLPREDNISOLONE	40 mg (milligram(s))	Other: EVERY 6 HOURS	Y-M: 20[redacted]- [redacted] / 162	Y-M: 20[redacted]- / 164
METRONIDAZOLE	500 mg (milligram(s))	Other: EVERY SIX HOURS	Y-M: 20[redacted]- [redacted] / 162	Y-M: 20[redacted]- / 165
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 162	Y-M: 20[redacted]- / 165
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 164	Y-M: 20[redacted]- / 165
LOPERAMIDE	4 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 164	Y-M: 20[redacted]- / 165
SACCHAROMYCES BOULARDII	250 mg (milligram(s))	BID	Y-M: 20[redacted]- [redacted] / 164	Y-M: 20[redacted]- / 186
LEVOFLOXACIN	500 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 166	Y-M: 20[redacted]- / 186
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 166	Y-M: 20[redacted]- / 186
METRONIDAZOLE	500 mg (milligram(s))	Other: EVERY SIX HOURS	Y-M: 20[redacted]- [redacted] / 166	Y-M: 20[redacted]- / 187
ACICLOVIR	800 mg (milligram(s))	TID	Y-M: 20[redacted]- [redacted] / 170	ONGOING
ASCORBIC ACID	500 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 186	ONGOING
CIPROFLOXACIN	400 mg (milligram(s))	Other: EVERY 12 HOURS	Y-M: 20[redacted]- [redacted] / 186	Y-M: 20[redacted]- / 188
MORPHINE	2-4 mg (milligram(s))	Other: EVERY 4 HOURS PRN	Y-M: 20[redacted]- [redacted] / 186	Y-M: 20[redacted]- / 193
ONDANSETRON	4 mg (milligram(s))	Other: EVERY 6 HOURS PRN	Y-M: 20[redacted]- [redacted] / 186	Y-M: 20[redacted]- / 193
ZOLPIDEM	10 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 186	Y-M: 20[redacted]- / 196
METRONIDAZOLE	500 mg (milligram(s))	Other: EVERY 8 HOURS	Y-M: 20[redacted]- [redacted] / 187	Y-M: 20[redacted]- / 190
PREDNISONE	10 mg (milligram(s))	BID	Y-M: 20[redacted]- [redacted] / 187	Y-M: 20[redacted]- / 191

FAMOTIDINE	20 mg (milligram(s))	BID	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 187 / 198
ENALAPRIL	1.25 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 188 / 188
TIGECYCLINE	1000 mg (milligram(s))	Other: EVERY 12 HOURS	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 188 / 190
LACTINEX	ONE TAB TAB	QD	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 188 / 192
IRON	200 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 190 / 190
VANCOMYCIN	250 mg (milligram(s))	Other: EVERY 6 HOURS	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 190 / 192
IRON	325 mg (milligram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 191 / 192
ZINC	TOPICAL OINTMENT APPLICATION	BID	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 192 / 199
BACITRACIN	ONE TOPICAL APPLICATION	Other: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 193 / 193
DESMOPRESSIN	20 mEq (milliequivalent(s))	Other: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 193 / 193
HYDROCORTISONE	100 mg (milligram(s))	Other: TODAY	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 193 / 193
MAGNESIUM SULFATE	1 g (gram(s))	Other: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 193 / 193
MIDAZOLAM	2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 193 / 193
HYDROMORPHONE	20 mg (milligram(s))	Other: VIA PCA PUMP CASSETTE	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 193 / 196
PARACETAMOL	1 g (gram(s))	Other: EVERY 6 HOURS	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 193 / 197
POTASSIUM	10 mEq (milliequivalent(s))	Other: AS NEEDED	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 193 / 198
FLUCONAZOLE	200 mg (milligram(s))	Other: EVERY TWENTY-FOUR HOURS	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 193 / 199
HYDROCORTISONE	75 mg (milligram(s))	Other: TODAY	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 194 / 194
METRONIDAZOLE	500 mg (milligram(s))	Other: EVERY 8 HOURS	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 194 / 199
ENOXAPARIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 194 / 200
ERTAPENEM	1 g (gram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted]-[redacted] / 194 / 200

LACTINEX	ONE TAB	QD	Y-M: 20[redacted]- ONGOING [redacted] / 195
HYDROCORTISONE	50 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 195 / 195
HYDROCORTISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 196 / 198
POTASSIUM	20 mEq (milliequivalent(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 196 / 199
OLANZAPINE	5 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 197 / 197
QUETIAPINE	25 mg (milligram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 197 / 199
FAMOTIDINE	20 mg (milligram(s))	BID	Y-M: 20[redacted]- ONGOING [redacted] / 199
PREDNISONE	10 mg (milligram(s))	BID	Y-M: 20[redacted]- ONGOING [redacted] / 199
SPIRONOLACTONE	25 mg (milligram(s))	QD	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 199 / 200
ERGOCALCIFEROL	400 IU (international unit(s))	QD	Y-M: 20[redacted]- ONGOING [redacted] / 200
LEKOVIT CA	500/200 mg (milligram(s))	QD	Y-M: 20[redacted]- ONGOING [redacted] / 200

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

Event Description	DEHYDRATION, ULCERATIVE COLITIS - WORSENING
Preferred term	潰瘍性大腸炎，脱水
AE Onset Date / Rx Day	[redacted]20[redacted] / 129 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	135 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	7 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	WORSENING OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES

SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	WORSENING ULCERATIVE COLITIS, IRON DEFICIENCY ANEMIA, THROMBOCYTOSIS, HYPONATREMIA
Preferred term	潰瘍性大腸炎，低ナトリウム血症，鉄欠乏性貧血，血小板増加症
AE Onset Date / Rx Day	[redacted]20[redacted] / 162 (35 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	165 (38 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	WORSENING OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 186 (59 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 193): TOTAL ABDOMINAL COLECTOMY WITH END ILEOS: STABLE	
AE Stopped Rx Day	200 (73 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility

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

Generated: [redacted] 20[redacted]:02:12
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の女性（米国）であり，重篤な有害事象の脱水及び潰瘍性大腸炎の悪化が認められた。関連する病歴は，左側潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，脱水及び潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，脱水及び潰瘍性大腸炎の悪化は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，腹痛，食欲減退，重度の下痢，脱力，及び脱水の症状を伴う潰瘍性大腸炎再燃が認められ，被験者は入院した。治療として静脈内水分補給が実施され，鎮痛剤が静脈内投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬としてヒドロコルチゾン，Dilaudid（ヒドロモルフォン塩酸塩），Protonix（パントプラゾールナトリウム水和物），ブデソニド，塩化カリウム，ヒドラジン，Zofran（オンダンセトロン塩酸塩水和物），Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム），アムロジピン，及びモルヒネ硫酸塩水和物が投与された。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Dehydration (10012174) (Dehydration (10012174)) [v.21.1] [10012174]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of DEHYDRATION

- Investigator: Worsening of ulcerative colitis

- AbbVie: Exacerbation of underlying disease of UC.

Event of ULCERATIVE COLITIS WORSENING

- Investigator: Worsening of ulcerative colitis.

- AbbVie: Exacerbation of underlying disease of UC.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，女性（米国）であり，重篤な有害事象の潰瘍性大腸炎の悪化，鉄欠乏性貧血，血小板増加症，及び低ナトリウム血症が認められた。関連する病歴は，左側潰瘍性大腸炎及びクロストリジウム・ディフィシレ感染であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化，鉄欠乏性貧血，血小板増加症，及び低ナトリウム血症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化，鉄欠乏性貧血，血小板増加症，及び低ナトリウム血症は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪，急性貧血，及び栄養失調が認められ，被験者は入院した。軟便・下痢が複数回みられ，脱力及び栄養失調の症状が認められた。ヘモグロビン値は 7.8，ナトリウム値は 130 であった。静脈内水分補給及び赤血球濃厚液投与（2 単位）が実施され，ステロイド剤が静脈内投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Florastor，Imodium（ロペラミド塩酸塩），Levaquin（レボフロキサシン水和物），Dilaudid（ヒドロモルフォン塩酸塩），Flagyl（メトロニダゾール），Protonix（パントプラゾールナトリウム水和物），Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム）及び prednisone が投与された。

The patient's past medications include:

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BUDESONIDE ER for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTOCORT EC for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

2) Iron deficiency anemia (10022974) (Iron deficiency anaemia (10022972)) [v.19.0] [10022974]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

3) Thrombocytosis (10043563) (Thrombocytosis (10043563)) [v.19.0] [10043563]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

4) Hyponatremia (10021038) (Hyponatraemia (10021036)) [v.19.0] [10021038]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of WORSENING ULCERATIVE COLITIS, IRON DEFICIENCY ANEMIA, THROMBOCYTOSIS, HYPONATREMIA

- Investigator: Worsening of Ulcerative Colitis.

- AbbVie: The event is worsening of underlying disease of UC.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の女性（米国）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，内痔核，潰瘍性大腸炎（左側潰瘍性大腸炎），及びクロストリジウム・ディフィシレ感染であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，急性憩室炎，潰瘍性大腸炎の症状悪化，及び高トランスアミナーゼ血症が認められ，被験者は入院した。便失禁，飲食不能，脱力，及び脱水を含む兆候及び症状が認められた。コンピュータ断層撮影検査の結果，大腸炎の所見が認められた。治療薬として抗生剤が投与された。20[redacted] 年 [redacted] 月 [redacted] 日，経腹的結腸全摘術が実施され，終末型回腸瘻が造設された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は容体が安定した状態でリハビリテーションのための療養施設へ転院した。

治療薬として Ambien（ゾルピデム酒石酸塩），Omirmev，Diflucan（フルコナゾール），Lovenox（エノキサパリンナトリウム），Dilaudid（ヒドロモルフォン塩酸塩），Solu-Cortef（ヒドロコルチゾンコハク酸エステルナトリウム），Invanz，塩化カリウム，バンコマイシン，硫酸鉄，Tygacil（チゲサイクリン），Floranex，Cipro（シプロフロキサシン），ファモチジン，Deltasone，Flagyl（メトロニダゾール），モルヒネ硫酸塩水和物，及び Zofran（オンダンセトロン塩酸塩水和物）が投与された。

The patient's past medications include:

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BUDESONIDE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BUDESONIDE ER for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTOCORT EC for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.22.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Dehydration.

- AbbVie: The event is exacerbation of underlying disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

The colonoscopy showed a result of the following: rectum had a result of 2 indicating moderate disease (marked erythema, absent vascular pattern, friability, erosions); sigmoid had a result of 1indicating mild disease (erythema, decreased vascular pattern, mild friability); descending colon, transverse colon and ascending colon/cecum had a result of 0 indicating normal or inactive disease; no presence of friability; and a subscore of 2.

[redacted] 20[redacted] CT: Evidence of colitis

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
会陰膿瘍	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	4[redacted]	MALE	White

Medical History	Onset Year
SURGERY: TONSILLECTOMY	19[redacted]
NEPHROLITHIASIS: USUALLY OCCURS EVERY 2 - 3 YEARS.	19[redacted]
ANEMIA: SECONDARY TO UC	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: ANXIETY	20[redacted]
OTHER: HIP PAIN SECONDARY TO UC	20[redacted]
OTHER: INSOMNIA SECONDARY TO PREDNISONE.	20[redacted]
OTHER: SKIN PUSTULES LIKELY ERYTHEMA NODOSUM, SECONDARY TO UC	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	5	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 50	50
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ALPRAZOLAM	0.5 mg (milligram(s))	PRN	Y-M: 20[redacted]
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted]
OMEPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
BALSALAZIDE	750 mg (milligram(s))	TID	Y-M: 20[redacted] / -300
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -300
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -300
IRON	65 mg (milligram(s))	QD	Y-M: 20[redacted] / -234
OXYCODONE	5 mg (milligram(s))	PRN	Y-M: 20[redacted] / -45
MACROGOL 3350	238 g (gram(s))	Other: MIXED WITH GATORADE AND CONSUMED OVER A 6 HOUR PERIOD.	Y-M: 20[redacted] / -41
FLEBOBAG RING LACT	300 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted] / -40
LIDOCAINE	50 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -40
PROPOFOL	15 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -40
CIPROFLOXACIN	400 mg (milligram(s))	BID	Y-M: 20[redacted] / -37
KETOROLAC	30 mg (milligram(s))	Other: ONCE ONLY	Y-M: 20[redacted] / -37
METRONIDAZOLE	500 mg (milligram(s))	QID	Y-M: 20[redacted] / -37
MORPHINE	4 mg (milligram(s))	BID	Y-M: 20[redacted] / -37

ONDANSETRON	4 mg (milligram(s))	BID	Y-M: 20[redacted] / -37
SODIUM CHLORIDE	1000 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted] / -37
CIPROFLOXACIN	400 mg (milligram(s))	BID	Y-M: 20[redacted] / -35

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ALPRAZOLAM	0.5 mg (milligram(s))	PRN	Y-M: 20[redacted]	ONGOING
OMEPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
BALSALAZIDE	750 mg (milligram(s))	TID	Y-M: 20[redacted] / -300	ONGOING
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -300	ONGOING
IRON	65 mg (milligram(s))	QD	Y-M: 20[redacted] / -234	ONGOING
OXYCODONE	5 mg (milligram(s))	PRN	Y-M: 20[redacted] / -45	ONGOING
TAMSULOSIN	0.4 mg (milligram(s))	QD	Y-M: 20[redacted] / 34	ONGOING
TRIAMCINOLONE	0.1 % (percent)	QD	Y-M: 20[redacted] / 204	ONGOING
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 249	Y-M: 20[redacted] / 258
ANESTHETICS, GENERAL	NOT REPORTED	Other: ONCE ONLY	Y-M: 20[redacted] / 264	Y-M: 20[redacted] / 264
LIDOCAINE	5 mL (millilitre(s))	Other: ONCE ONLY	Y-M: 20[redacted] / 264	Y-M: 20[redacted] / 264
CLINDAMYCIN	300 mg (milligram(s))	QID	Y-M: 20[redacted] / 264	Y-M: 20[redacted] / 279

Event #1: Serious Adverse Event

Event Description	PERINEAL ABSCESS
Preferred term	会陰膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 264
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 264): EXCISION: N/A [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 264): DEBRIDEMENT OF PERINEAL ABSCESS: PERINEAL ABSCESS, SUPERFICIAL

AE Stopped Rx Day	264
Duration of AE	1 DAY
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NORMAL DISEASE PROGRESSION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（米国）であり，重篤な有害事象の会陰膿瘍が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，会陰膿瘍が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，会陰膿瘍は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，肛門周囲痛が認められ，治療薬として Cipro（シプロフロキサシン）500 mg が 1 日 2 回，10 日間投与された結果，回復した。疼痛は再燃し，被験者は救急治療室の受診を指示された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，切除術及び会陰膿瘍デブリドマンが実施された。

治療薬としてクリンダマイシンが投与された。

Causality for HUMIRA (Open Label)

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1) Perineal abscess (10052457) (Perineal abscess (10052457)) [v.18.0] [10052457]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of PERINEAL ABSCESS

- Investigator: Normal disease progression

- AbbVie: The event is exacerbation of underlying disease

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
子宮平滑筋腫	X			
潰瘍性大腸炎	X	X		
心房細動		X		
小腸炎		X		
術後高血圧		X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	4[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: ORAL SURGERY	19[redacted]
DEPRESSION: DEPRESSION	19[redacted]
SURGERY: BREAST AUGMENTATION	20[redacted]
OTHER: UTERINE FIBROID	20[redacted]
SURGERY: INGUINAL HERNIA REPAIR	20[redacted]
SURGERY: MYOMECTOMY	20[redacted]
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
VALVULAR HEART DISEASE: MV PROLAPSE	20[redacted]
OTHER: ALLERGY TO PERCODONE	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 55	[redacted]20[redacted] / 83	29

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DULOXETINE	60 mg (milligram(s))	QD	Y-M: 20[redacted]
CILEST	1 TABLET	QD	Y-M: 20[redacted]
IRON	325 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -116
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -78
METHOTREXATE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -58

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
DULOXETINE	60 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
CILEST	1 TABLET	QD	Y-M: 20[redacted]	ONGOING
IRON	325 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -116	ONGOING
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -78	Y-M: 20[redacted]-[redacted] / 28
IRON	750 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 27	Y-M: 20[redacted]-[redacted] / 27
BUDESONIDE	4.5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 29	Y-M: 20[redacted]-[redacted] / 42
BUDESONIDE	3 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 43	Y-M: 20[redacted]-[redacted] / 55
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 56	Y-M: 20[redacted]-[redacted] / 89
METHYLPREDNISOLONE	20 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 87	Y-M: 20[redacted]-[redacted] / 90

TRIAMCINOLONE	0.025 % (percent)	QD	Y-M: 20[redacted]-[redacted] ONGOING / 89
IRON	300 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 89 92
CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 91 92
COLECALCIFEROL	400 IU (international unit(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 91 92
ERGOCALCIFEROL	50000 IU (international unit(s))	Other: WEEKLY	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 91 92
DEXAMETHASONE	4 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
FAMOTIDINE	20 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
FENTANYL	250 mcg (microgram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
FLEBOBAG RING LACT	2600 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
GLYCOPYRRONIUM	0.4 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
HYDROMORPHONE	2 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
LIDOCAINE	70 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
METOCLOPRAMIDE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
MIDAZOLAM	2 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
NEOSTIGMINE	3 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
ONDANSETRON	4 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
PROPOFOL	150 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
ROCURONIUM	110 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
SUXAMETHONIUM	80 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 93 93
SODIUM CHLORIDE	0.9 % (percent)	Other: CONTINUOUS	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 94 96
VICODIN	325 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] Y-M: 20[redacted]-[redacted] / / 97 105

LOPERAMIDE	1 mg (milligram(s))	QID	Y-M: 20[redacted]-[redacted] / 97 Y-M: 20[redacted]-[redacted] / 107
SENNOSIDE A+B	100 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 98 Y-M: 20[redacted]-[redacted] / 98
GLUCOSE	5 % (percent)	QD	Y-M: 20[redacted]-[redacted] / 100 Y-M: 20[redacted]-[redacted] / 100
METOCLOPRAMIDE	10 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / 100 Y-M: 20[redacted]-[redacted] / 104
SIMETICONE	160 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / 100 Y-M: 20[redacted]-[redacted] / 108
TRAMADOL	50 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 102 Y-M: 20[redacted]-[redacted] / 139
PLANTAGO OVATA	6 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / 104 ONGOING
DILTIAZEM	15 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / 104 Y-M: 20[redacted]-[redacted] / 105
SODIUM PHOSPHATE	0.9 % (percent)	QD	Y-M: 20[redacted]-[redacted] / 104 Y-M: 20[redacted]-[redacted] / 105
PROCHLORPERAZINE	10 mg (milligram(s))	QID	Y-M: 20[redacted]-[redacted] / 104 Y-M: 20[redacted]-[redacted] / 108
DIPHENHYDRAMINE	25 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / 105 Y-M: 20[redacted]-[redacted] / 109
ENOXAPARIN	40 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 105 Y-M: 20[redacted]-[redacted] / 109
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 105 Y-M: 20[redacted]-[redacted] / 109
NALOXONE	200 mcg (microgram(s))	PRN	Y-M: 20[redacted]-[redacted] / 105 Y-M: 20[redacted]-[redacted] / 109
PARACETAMOL	650 mg (milligram(s))	QID	Y-M: 20[redacted]-[redacted] / 105 Y-M: 20[redacted]-[redacted] / 109
CIPROFLOXACIN	400 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 105 Y-M: 20[redacted]-[redacted] / 115
FENTANYL	50 mcg (microgram(s))	QD	Y-M: 20[redacted]-[redacted] / 106 Y-M: 20[redacted]-[redacted] / 106
MIDAZOLAM	2 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 106 Y-M: 20[redacted]-[redacted] / 106
METHYLPREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 106 Y-M: 20[redacted]-[redacted] / 107
POTASSIUM	20 mEq (milliequivalent(s))	QD	Y-M: 20[redacted]-[redacted] / 107 Y-M: 20[redacted]-[redacted] / 107
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / 107 Y-M: 20[redacted]-[redacted] / 108

SODIUM CHLORIDE	0.9 % (percent)	Other: CONTINUOUS	Y-M: 20[redacted]-[redacted] / / 107 Y-M: 20[redacted]-[redacted] / / 108
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / / 108 Y-M: 20[redacted]-[redacted] / / 108
ERGOCALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted]-[redacted] / / 109 ONGOING
LISINOPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / / 149 Y-M: 20[redacted]-[redacted] / / 223

Event #1: Serious Adverse Event

Event Description	UTERINE FIBROID
Preferred term	子宮平滑筋腫
AE Onset Date / Rx Day	[redacted]20[redacted] / 56
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
(RX DAY): OUTPATIENT TOTAL LAPAROSCOPIC HYSTERECT: SUBJECT TOLERATED PROCEDURE WELL WITHOUT COMPLICATIONS. TOLERATING REGULAR DIET, PAIN UNDER CONTROL, NO BLEEDING POST-OP. PATHOLOGY REPORT STATES UTERUS, CERVIX, BILATERAL FALLOPIAN TUBES, HYSTERECTOM	
AE Stopped Rx Day	57
Duration of AE	2 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UTERINE FIBROIDS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	WORSENING ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 87 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 87): ALBUMIN: 34 [35 - 57] G/L; C REACTIVE PROTEIN: 5.3 [0 - 0.5] MG/DL; HEMOGLOBIN: 114 [116 - 154] G/L; SEDIMENTATION RATE: 30 [2 - 25] MM/HOUR; VITAMIN D 25 HYDROXY: 16.6 [30 - 100] NG/ML; [redacted]20[redacted] (RX DAY 88): IRON: 24 [50 - 212] UG/DL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 87): XR ABDOMEN AP/LAT: LOSS OF HAUSTRAL MARKINGS WITHIN THE DESCENDING AND SIGMOID COLON IS CONSISTENT WITH PATIENT'S HISTORY OF ULCERATIVE COLITIS.; [redacted]20[redacted] (RX DAY 93): FULL COLECTOMY WITH END ILEOSTOMY: POST-OP COURSE WAS COMPLICATED BY ABDOMINAL PAIN, HIGH OSTOMY OUTPUT WITH EVIDENCE OF POST-COLECTOMY ENTERITIS AND NEW ONSET ATRIAL FIBRILLATION WITH RVR.; [redacted]20[redacted] (RX DAY 106): ILEOSCOPY: MODERATE TO SEVERELY ACTIVE ILEITIS. DIFFERENTIAL INCLUDES ILEAL CROHN'S DISEASE VS POST-COLECTOMY ENTERITIS VS CMV ENTERITIS.

AE Stopped Rx Day	109 (26 DAYS AFTER LAST TREATMENT)
Duration of AE	23 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	WORSENING ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: AE Leading to Discontinuation of Study Drug

Event Description	NEW ONSET ATRIAL FIBRILLATION
Preferred term	心房細動
AE Onset Date / Rx Day	[redacted]20[redacted] / 104 (21 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #4: AE Leading to Discontinuation of Study Drug

Event Description	POST-COLECTOMY ENTERITIS
Preferred term	小腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 106 (23 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #5: AE Leading to Discontinuation of Study Drug

Event Description	HYPERTENSION IN THE CONTEXT OF POST-OPERATIVE CATECHOLAMINES
Preferred term	術後高血圧
AE Onset Date / Rx Day	[redacted]20[redacted] / 149 (66 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	223 (140 DAYS AFTER LAST TREATMENT)
Duration of AE	75 DAYS
Severity	Mild
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]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（米国）であり，重篤な有害事象の子宮筋腫が認められた。関連する病歴は，潰瘍性大腸炎及び子宮筋腫であり，筋腫摘出の手術歴があった。
20[redacted] 年 [redacted] 月 [redacted] 日，子宮筋腫が認められた。同日に被験者は入院した。月経過多，疼痛を伴う重度の月経，及び非常に大きな筋腫に関連した骨盤圧を含む症状が認められた。予定されていた外来外科手術により腹腔鏡下子宮全摘術が実施された。被験者は鉄欠乏性貧血及びヘモグロビン低値の病歴を有していたため入院し，術後モニタリングが行われた。手術の忍容性は良好で，合併症はみられなかった。夜間モニタリングでは特筆すべき点はなかった。疼痛は良好に管理されており，静脈内薬剤投与は最小限であった。バイタルサインは安定していた。20[redacted] 年 [redacted] 月 [redacted] 日，子宮筋腫は回復した。同日に被験者は容体が安定した状態で退院した。
治療薬として Uceris（ブデソニド）が投与された。

The patient's past medications include:

METHOTREXATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PERCODONE for UNKNOWN INDICATION

Causality for HUMIRA (Open Label)

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1) Uterine fibroid (10046783) (Uterine leiomyoma (10046798)) [v.18.0] [10046783]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No

Alternative Etiology for HUMIRA (Open Label)

Event of UTERINE FIBROID

- Investigator: POST-OP MONITORING

- AbbVie: Subject with previous history of uterine fibroids, went through hysterectomy

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（米国）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎，子宮筋腫，及び鼠径部ヘルニア修復であり，筋腫摘出の手術歴があった。被験者は非喫煙者であり，元アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月以降，潰瘍性大腸炎は良好に管理されていた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は潰瘍性大腸炎再燃のため入院した。また，被験者は背部痛，うつ病，四肢の発疹，及び消化器症状を訴えた。過去 2 週間の間に排便頻度の増加及び嘔吐が認められており，現時点での 1 日当たりの排便回数は 15～20 回で，腹部中央の鈍痛を伴っていた。過去 2 週間以前には，被験者から潰瘍性大腸炎再燃及び症状に伴う疼痛の発現歴はなかったとの報告があった。便の色は様々で，通常は血液が混じった軟便であった。被験者は頻繁な排便及び便意切迫を訴えた。被験者から，過去 2 週間の間に「排泄の失敗」が頻繁にあったとの報

告があった。[redacted] 月／[redacted] 月以降，体重が 10 ポンド減少していた。また，被験者はふらつき，疲労，及び不定期な労作時の息切れを訴えた。

20[redacted] 年 [redacted] 月 [redacted] 日，血便が 17 回認められ，低残渣食に耐性がみられた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は試験を中止し，同日に 10～15 回の血便が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，結腸全摘術が実施され，終末型回腸瘻が造設された。術後の経過において，合併症として腹痛，結腸全摘術後小腸炎の所見を伴うストーマ排液量過多，及び頻回心室応答を伴う心房細動発現が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，回腸内視鏡検査の結果，中等度から重度の活動性回腸炎が認められた。鑑別疾患には，回腸クローン病，結腸全摘術後小腸炎，及びサイトメガロウイルス小腸炎が含まれる。

治療薬としてコレカルシフェロール，エルゴカルシフェロール，トリアムシノロン，ヒドロモルフォン，乳酸リンゲル液，デキサメタゾン，Narcan（ナロキソン塩酸塩），フェンタニル，グリコピロニウム臭化物，リドカイン，メトクロプラミド，ミダゾラム，ネオスチグミン，オンダンセトロン，プロポフォール，rocuronium，succinylcholine，Metamucil，シプロフロキサシン，Tylenol，エノキサパリン，メトロニダゾール，Benadryl，沈降炭酸カルシウム，iron sucrose，Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム），ファモチジン，及びステロイドが投与された。

The patient's past medications include:

METHOTREXATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PERCODONE for UNKNOWN INDICATION

Causality for HUMIRA (Blinded)

---

1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.22.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of WORSENING ULCERATIVE COLITIS

- Investigator: Worsening ulcerative colitis

- AbbVie: The subject presented with worsening of ulcerative colitis. The subject is in a late postoperative period for uterine fibroids, and has stayed 2 weeks without the study drug as recommended for elective surgeries in the protocol.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] albumin: 3.4 G/DL (normal 3.5 to 5.7)

[redacted] 20[redacted] CRP: 5.3 mg/dL (normal 0.0 to 0.5)

[redacted] 20[redacted] Hemoglobin: 11.4 G/DL (normal 11.6 to 15.4)

[redacted] 20[redacted] Iron: 24 ug/dl (normal 50 to 212)

[redacted] 20[redacted] stool culture: negative for D Diff.

[redacted] 20[redacted] stool studies: negative for toxic megacolon

[redacted] 20[redacted] XRAY ABDOMEN AP/LAT:

loss of haustral markings within the decending and sigmoid colon consistent with a history of ulcerative colitis.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	7[redacted]	MALE	White

Medical History	Onset Year
OTHER: SHOULDER PAIN	19[redacted]
ARTHRALGIA	20[redacted]
SURGERY: LEFT TOTAL KNEE REPLACEMENT	20[redacted]
OTHER: HYPERCHOLESTEROLEMIA	20[redacted]
OTHER: ENLARGED PROSTATE	20[redacted]
OTHER: FATIGUE	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	30	20[redacted]
CIGARS	NEVER			
PIPES	FORMER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 360	305

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 19[redacted]
AZATHIOPRINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]
HYALURONIC ACID	20 mg (milligram(s))	Other: TWICE WEEKLY	Y-M: 20[redacted]
ALFUZOSIN	10 mg (milligram(s))	QD	Y-M: 20[redacted]
CALCIUM WITH VITAMIN D	600 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted]
VITAMINS NOS	1 TABLET	QD	Y-M: 20[redacted]
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -20
BISACODYL	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
MACROGOL 3350	238 g (gram(s))	QD	Y-M: 20[redacted] / -13
FENTANYL	75 mcg (microgram(s))	QD	Y-M: 20[redacted] / -12
MIDAZOLAM	3 mg (milligram(s))	QD	Y-M: 20[redacted] / -12

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 (milligram(s))	PRN	Y-M: 19[redacted]	ONGOING
HYALURONIC ACID	20 mg (milligram(s))	Other: TWICE WEEKLY	Y-M: 20[redacted]	ONGOING
ALFUZOSIN	10 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
CALCIUM WITH VITAMIN D	600 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
VITAMINS NOS	1 TABLET	QD	Y-M: 20[redacted]	ONGOING
FINASTERIDE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 303	ONGOING

ANESTHETICS, GENERALUN UN		PRN	Y-M: 20[redacted] / Y-M: 20[redacted] / 361 361
VICODIN	7.5/325 mg (milligram(s))	TID	Y-M: 20[redacted] / Y-M: 20[redacted] / 384 361

Event #1: Serious Adverse Event

Event Description	CHRONIC RIGHT SHOULDER JOINT PAIN
Preferred term	関節痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 361 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
(RX DAY): RIGHT TOTAL SHOULDER ARTHROPLASTY AND RI: SUCCESSFUL SURGERY WITH IMPROVED MOBILITY OF THE JOINT AND RECOVERING WITH A CLEAN DRY AND INTACT SURGICAL INCISION AND NO WARMTH OR ERYTHMA, NO SIGNS OF INFECTION. NEUOVASCULAR EXAM IS STABLE	
AE Stopped Rx Day	362 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	2 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	CHRONIC JOINT PAIN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，7[redacted] 歳の男性（米国）であり，重篤な有害事象の慢性的な右肩関節痛が認められた。関連する病歴は，肩痛及び関節痛であり，人工左膝関節置換術の手術歴があった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 30 年）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，慢性的な右肩関節痛が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，慢性的な右肩関節痛は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肩痛を訴え，入院した。被験者は，可動域及び機能の喪失を伴った長年にわたる進行性の肩痛歴を有していた。臨床検査及び X 線検査の結果，進行性の変形性肩関節症の所見が認められた。被験者の症状は，保存療法ではもはや管理できていなかった。長期的な疼痛緩和及び上肢機能回復を目的として，被験者は人工肩関節置換術に進むことを選択した。20[redacted] 年 [redacted] 月 [redacted] 日，人工右肩関節全置換手術及び右上腕二頭筋腱固定術が実施された。手術は成功し，関節の可動性が改善した。切開痕は清潔かつ乾燥していた。熱感及び紅斑はなく，感染の兆候もみられなかった。神経血管系の検査結果は安定していた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Norco hydrocodo -acetaminophen が投与された。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted] [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [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 HUMIRA 40MG/0.8ML (Open Label)

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1) Arthralgia (10003239) (Arthralgia (10003239)) [v.19.0] [10003239]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of CHRONIC RIGHT SHOULDER JOINT PAIN

- Investigator: Chronic joint pain

- AbbVie: The subject has known medical history of the shoulder joint pain.

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	6[redacted]	MALE	White

Medical History	Onset Year
SURGERY: RIGHT ANKLE AND HIP DUE TO MVA	19[redacted]
DIABETES MELLITUS: ON ORAL MEDICATION	19[redacted]
HYPERTENSION: HIGH BLOOD PRESSURE ON MEDICATION	19[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: HEARTBURN	20[redacted]
OTHER: BARRETT'S ESOPHAGUS	20[redacted]
CHOLELITHIASIS: CHOLECYSTECTOMY	NOT REPORTED
SURGERY: PROSTATECTOMY	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACKS	30	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 54	[redacted]20[redacted] / 77	24

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg (milligram(s))	QD	Y-M: 19[redacted]
FISH OIL	1200 mg (milligram(s))	QD	Y-M: 19[redacted]
VITAMINS NOS	1 TABLET	QD	Y-M: 19[redacted]
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
ALLIUM SATIVUM	1100 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1.2 g (gram(s))	QID	Y-M: 20[redacted]
IRON	65 mg (milligram(s))	QD	Y-M: 20[redacted]
METFORMIN	500 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / -290
LISINOPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -229
INFLIXIMAB	500 mg (milligram(s))	Other: ONCE A MONTH	Y-M: 20[redacted]-[redacted] / -162
CLOBETASOL	1 APPLICATION 0.05 % (percent)	BID	Y-M: 20[redacted]-[redacted] / -48
FENTANYL	50 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -8
FLEET	2 ENEMAS	Other: ONCE	Y-M: 20[redacted]-[redacted] / -8
MIDAZOLAM	2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[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
ACETYLSALICYLIC ACID	81 mg (milligram(s))	QD	Y-M: 19[redacted]	ONGOING
FISH OIL	1200 mg (milligram(s))	QD	Y-M: 19[redacted]	ONGOING
VITAMINS NOS	1 TABLET	QD	Y-M: 19[redacted]	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
ALLIUM SATIVUM	1100 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	1.2 g (gram(s))	QID	Y-M: 20[redacted]	ONGOING
IRON	65 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
METFORMIN	500 mg (milligram(s))	TID	Y-M: 20[redacted] / -290	ONGOING
LISINOPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -229	ONGOING
CLOBETASOL	1 APPLICATION 0.05 % (percent)	BID	Y-M: 20[redacted] / -48	ONGOING
FENTANYL	75 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 54
MIDAZOLAM	3 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 54
METHYLPREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 87
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 88	ONGOING

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

Event Description	WORSENING UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 84 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 85): FLEXIBLE SIGMOIDOSCOPY: LOSS OF VASCULARITY, GRANULAR PATTERN, ERYTHEMA, AND SUPERFICIAL EROSION AND ULCERATIONS NOTED THROUGHOUT THE VISUALIZED COLON CONSISTENT WITH SEVERELY ACTIVE UC

AE Stopped Rx Day	152 (75 DAYS AFTER LAST TREATMENT)
Duration of AE	69 DAYS

Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	INEFFECTIVE TREATMENT WITH STUDY MEDICATION.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（米国）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。
排便頻度の増加及び直腸出血が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は潰瘍性大腸炎再燃，内視鏡検査，及び治療薬として Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム）の静脈内投与のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，prednisone 投与は漸減され，被験者は容体が安定した状態で退院した。
治療薬として Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム）及び prednisone が投与された。

Causality for HUMIRA (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.22.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of WORSENING UC

- Investigator: Ineffective treament with study medication.

- AbbVie: The event is exacerbation of underlying disease of UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Flexible sigmoidoscopy:

Loss of vascularity, granular pattern, erythema, superficial erosion and ulcerations noted throughout the visualized colon consistent with severely active UC.

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			
悪心	X			
嘔吐	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK2[redacted]		FEMALE	White

Medical History	Onset Year
HYPERTENSION	20[redacted]
ANEMIA: IRON DEFICIENCY	20[redacted]
DEPRESSION: SELF EXPLANATORY	20[redacted]
OTHER: ELEVATED LIVER FUNCTION TESTS	20[redacted]
OTHER: POLYCYSTIC OVARIES	20[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
PRIMARY SCLEROSING CHOLANGITIS	20[redacted]
ARTHRALGIA	20[redacted]
OTHER: HEADACHES	20[redacted]
OTHER: HIRSUTISM FACE/BACK	20[redacted]
OTHER: SMALL INFECTION RIGHT BUTTOCK	20[redacted]
OTHER: TRUNKAL OBESITY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted] / 1	[redacted] / 28	28
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted] / 57	[redacted] / 161	105

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
CILEST	1 TABLET	QD	Y-M: 20[redacted]
ESCITALOPRAM	10 mg (milligram(s))	BID	Y-M: 20[redacted]
LISINOPRIL	20 mg (milligram(s))	QD	Y-M: 20[redacted]
MUPIROCIN	2% % (percent)	TID	Y-M: 20[redacted] / -57
FOLIC ACID	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -22

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
CILEST	1 TABLET	QD	Y-M: 20[redacted]	ONGOING
ESCITALOPRAM	10 mg (milligram(s))	BID	Y-M: 20[redacted]	ONGOING
LISINOPRIL	20 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
FOLIC ACID	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -22	ONGOING
IRON	65 mg (milligram(s))	BID	Y-M: 20[redacted] / 86	ONGOING
DOXYCYCLINE	100 mg (milligram(s))	BID	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 100
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 100
CLOTRIMAZOLE	1 APPLICATION/SPRINKLE	BID	Y-M: 20[redacted] / 111	ONGOING

FAMOTIDINE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 125
PROMETHAZINE	25 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 125
MORPHINE	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 126
CEFTRIAXONE	1 g (gram(s))	BID	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 127
HYDROMORPHONE	1 mg (milligram(s))	PRN	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 130
ONDANSETRON	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 130
OSMOTAN	20 mEq (milliequivalent(s))	TID	Y-M: 20[redacted] / 126	Y-M: 20[redacted] / 130
OXYCOCET	2 TABLETS	PRN	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 130
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 130

Event #1: Serious Adverse Event

Event Description	INTRACTABLE ABDOMINAL PAIN
Preferred term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 125
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 125): CT SCAN ABDOMEN AND PELVIS: NO ACUTE ABDOMINAL OR PELVIC PROCESS	
AE Stopped Rx Day	130
Duration of AE	6 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	GASTRITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	INTRACTABLE NAUSEA AND VOMITING
Preferred term	悪心，嘔吐
AE Onset Date / Rx Day	[redacted]20[redacted] / 125
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	130
Duration of AE	6 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	GASTRITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（米国）であり，重篤な有害事象の難治性の腹痛，並びに難治性の悪心及び嘔吐が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型），肝機能検査値の上昇，原発性硬化性胆管炎，及び多嚢胞性卵巣であった。

20[redacted] 年 [redacted] 月 [redacted] 日，難治性の腹痛，並びに難治性の悪心及び嘔吐が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，難治性の腹痛，並びに難治性の悪心及び嘔吐は回復した。悪心，嘔吐，及び左下腹部に疼痛が認められ，疼痛の強さは 10 段階中 8 であった。20[redacted] 年 [redacted] 月 [redacted] 日の入院以降，被験者は経口による食事に耐性がなく，1 日当たり 15～20 回の下痢が認められたが，軟便はみられなかっ

た。治療として静脈内水分補給，制吐剤投与，抗生剤の予防的投与，及び鎮痛管理が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Zofran（オンダンセトロン塩酸塩水和物），セフトリアキソン，モルヒネ，Percocet，メトロニダゾール，生理食塩水及び塩化カリウムを含む 5%ブドウ糖液，Phenergan（プロメタジン塩酸塩），Pepcid（ファモチジン），Dilaudid（ヒドロモルフォン塩酸塩），及び Rocephin 静注用（セフトリアキソンナトリウム水和物）が投与された。

The patient's past medications include:

MUPIROCIN OINTMENT for INFECTED AREA RIGHT BUTTOCK ([redacted] 20[redacted] - [redacted] 20[redacted])

ADOXA for PELVIC INFECTION [redacted] 20[redacted] - [redacted] 20[redacted])

BACTRIM DS for URINARY TRACT INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted])

METRONIDAZOLE for PELVIC INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Abdominal pain (10000081) (Abdominal pain (10000081)) [v.19.1] [10000081]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2) Nausea (10028813) (Nausea (10028813)) [v.19.1] [10028813]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

3) Vomiting (10047700) (Vomiting (10047700)) [v.19.1] [10047700]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of INTRACTABLE ABDOMINAL PAIN

- Investigator: Gastritis

- AbbVie: The event is reported as of bacterial causality

Event of INTRACTABLE NAUSEA AND VOMITING

- Investigator: Gastritis

- AbbVie: The event is likely of bacterial causality.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Rectum and sigmoid: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Descending colon, Transverse colon, Ascending colon/cecum: 0 = Normal or inactive disease

Friability subscore 2

[redacted] 20[redacted] CT scan of abdomen and pelvis: No acute abdominal or pelvic process

[redacted] 20[redacted] Flexible sigmoidoscopy:

Rectum, sigmoid, descending colon, Transverse colon, Ascending colon/cecum: 0 = Normal or inactive disease

Friability subscore 2

Unknown date Stool studies: 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
潰瘍性大腸炎	X	X		
敗血症	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	4[redacted]	MALE	White

Medical History	Onset Year
PYODERMA GANGRENOSUM: LOCATION ON RIGHT LEG.	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	UNKNOWN			
CIGARETTES	FORMER	0 PACKS	5	20[redacted]
CIGARS	UNKNOWN			
PIPES	UNKNOWN			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 40	40
ADALIMUMAB TDM	40/40/160/40 MG	EOW/EW/EW/EW	[redacted]20[redacted] / 55	[redacted]20[redacted] / 196	142

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HYDROCODONE	325 mg (milligram(s))	Other: TID - QID	Y-M: 20[redacted]
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]
INFLIXIMAB	700 mg (milligram(s))	Other: EVERY 8 WEEKS	Y-M: 20[redacted] / -333
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -277
CURCUMA LONGA	450 mg (milligram(s))	QD	Y-M: 20[redacted] / -63
CYANOCOBALAMIN	1000 mcg (microgram(s))	QD	Y-M: 20[redacted] / -63
LINUM USITATISSIMUM	1400 mg (milligram(s))	QD	Y-M: 20[redacted] / -63
BACTRIM	160 mg (milligram(s))	QD	Y-M: 20[redacted] / -15
SUPREP BOWEL PREP	MULTIPLE INGREDIENTS mg (milligram(s))	QD	Y-M: 20[redacted] / -10
HYOSCYAMINE	0.75 mg (milligram(s))	BID	Y-M: 20[redacted] / -8
VICODIN	10-325 mg (milligram(s))	PRN	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
HYDROCODONE	325 mg (milligram(s))	Other: TID - QID	Y-M: 20[redacted]	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -277	ONGOING
CURCUMA LONGA	450 mg (milligram(s))	QD	Y-M: 20[redacted] / -63	ONGOING
CYANOCOBALAMIN	1000 mcg (microgram(s))	QD	Y-M: 20[redacted] / -63	ONGOING
LINUM USITATISSIMUM	1400 mg (milligram(s))	QD	Y-M: 20[redacted] / -63	ONGOING
HYOSCYAMINE	0.75 mg (milligram(s))	BID	Y-M: 20[redacted] / -8	ONGOING
VICODIN	10-325 mg (milligram(s))	PRN	Y-M: 20[redacted] / -8	ONGOING
PREDNISONE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / 96	ONGOING
AMOXICILLIN	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 188	Y-M: 20[redacted] / 198
NOREPINEPHRINE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 201	Y-M: 20[redacted] / 204
PIP/TAZO	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 201	Y-M: 20[redacted] / 204
STEROIDS	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] /	Y-M: 20[redacted] / 204

			201	
VANCOMYCIN	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / 201	Y-M: 20[redacted] / 204
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 211

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

Event Description	FLARE OF ULCERATIVE COLITIS, SEPSIS SECONDARY TO ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎，敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 200 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 201): Stool ENTERIC PATHOGENS: N; Stool C-DIFF: N; Stool GIARDIA/CRYPTOSPORIDIUM ANTIGEN: N; Stool PARASITOLOGY STAIN: N; Stool FECAL LACTOFERRIN: P

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 201): CT ABDOMEN AND PELVIS: MILD EDEMA IN THE ANTERIOR PERINEPHRIC SPACE ON THE LEFT WHICH CAN BE SEEN WITH PANCREATITIS HOWEVER NO OBVIOUS PANCREATIC ABNORMALITY IS SEEN. CORRELATE WITH AMYLASE AND LIPASE LEVELS. GALLBLADDER I

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（米国）であり，重篤な有害事象の潰瘍性大腸炎再燃及び潰瘍性大腸炎再燃に続発する敗血症が認められた。関連する病歴は，壊疽性膿皮症（右足）及び潰瘍性大腸炎であった。被験者は元喫煙者（1 日当たり 0 箱，喫煙期間 5 年）であり，非アルコール摂取者であった。

本被験者への治験薬投与は，試験デザインをより良く反映させるために非盲検下投与から盲検下投与へ修正された。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃及び潰瘍性大腸炎再燃に続発する敗血症が認められた。

本事象の発現前には，連鎖球菌性咽頭炎（非重篤）が認められていた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は主治医に発熱及び頻脈を訴えた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は救急治療室を受診し，1 日の最高体温は 39.4°C であった。被験者は食欲不振及び放散性の腹痛により数日にわたって体調が優れず，全身の疼痛を訴えた。1 日当たり最大 10～12 回の慢性的な下痢（潰瘍性大腸炎）の現病歴があり，本事象の発現により変化はなかったが，被験者から少量の血液が認められたとの報告があった。被験者によると，排尿症状又は直近の体重減少はなかった。

救急治療室における身体的診察及びバイタルサイン：体温 37.6°C，心拍数 117 bpm，呼吸数 18 bpm，血圧 104/52 mmHg，酸素飽和度 100%（室内気）であった。腹部：柔らかく，腹部の広い範囲に軽度の圧痛が認められ，反跳圧痛又は筋性防御はみられなかった。腸蠕動音が聴取された。

治験責任医師による評価及び計画：1. おそらく敗血症性ショック状態である敗血症。被験者は受診時に敗血症がみられ，低血圧の状態であり，体液量減少及び過去に投与されたモルヒネによる可能性が認められた。輸液ボーラス投与が多数回行われたが，血圧は低いままであった。被験者は集中治療室へ移送され，Levophed の投与が必要となった。救急治療室においてバンコマイシン及び Zosyn（タゾバクタム／ピペラシリン水和物）を含む抗生剤投与が開始され，投与は継続された。2. 潰瘍性大腸炎。被験者は prednisone を長期間投与されており，低血圧の症状を有していたため，ストレス量のステロイド静脈内投与へ切り替えられた。クロストリジウム・ディフィシレ検査用に便が採取された。

被験者は集中治療室へ移送後，Levophed 投与が開始され，広範囲の抗生剤投与が継続された。腹部のコンピュータ断層撮影（以下「CT」）検査の結果，腹腔内膿傷は認められなかった。被験者は感染症科及び消化器内科を受診し，広範囲抗生剤及び Levophed の投与，並びに静脈内輸液及び静脈内ステロイド投与が行われた。症状は翌数日のうちに改善した。便中ラクトフェリン検査の結果は陽性であった。他の全ての便分析結果は陰性であった。白血球数は通常値に戻った。CT 検査の結果，胆嚢の腫大が認められた。超音波検査に引き続き，肝胆道シンチグラフィーが実施されたが，急性胆嚢炎の所見は認められなかった。容体が安定した後に，被験者は集中治療室から転出し，退院に向けてその後の手配が整えられた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてバンコマイシン，Zosyn（タゾバクタム／ピペラシリン水和物），Lovephed，Flagyl（メトロニダゾール），及びモルヒネが投与された。

The patient's past medications include:

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.22.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Sepsis secondary (10040053) (Sepsis (10040047)) [v.22.0] [10040053]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of FLARE OF ULCERATIVE COLITIS, SEPSIS SECONDARY TO ULCERATIVE COLITIS FLARE

- Investigator: Not applicable.

- AbbVie: Exacerbation of underlying disease.

Relevant Laboratory & Other Diagnostic Tests

Unknown date ABDOMINAL ULTRASOUND: DID NOT SHOW ANY EVIDENCE OF ACUTE CHOLECYSTITIS

[redacted] 20[redacted] BLOOD PRESSURE: 104/52 mmHg

[redacted] 20[redacted] BODY TEMPERATURE: 99.6 F

[redacted] 20[redacted] BODY TEMPERATURE: 103 F

[redacted] 20[redacted] CT ABDOMEN AND PELVIS: MILD EDEMA IN THE ANTERIOR PERINEPHRIC SPACE ON THE LEFT WHICH CAN BE SEEN WITH PANCREATITIS HOWEVER NO OBVIOUS PANCREATIC ABNORMALITY IS SEEN. CORRELATE WITH AMYLASE AND LIPASE LEVELS. GALLBLADDER IS DISTENDED NO DEFINITE GALLBLADDER INFLAMMATION. LARGE BOWEL IS FILLED WITH FLUID WHICH CAN BE SEE WITH LOW-GRADE COLITIS OR OTHER CAUSE OF DIARRHEA. CORRELATE WITH CLINICAL HISTORY

[redacted] 20[redacted] FECAL LACTOFERRIN: Postive

[redacted] 20[redacted] HEART RATE: 117 BPM

Unknown date HIDA SCAN: DID NOT SHOW ANY EVIDENCE OF ACUTE CHOLECYSTITIS

[redacted] 20[redacted] OXYGEN SATURATION: 100 %

[redacted] 20[redacted] RESP RATE: 18 breaths per minute

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

[redacted] 20[redacted] STOOL ENTERIC PATHOGENS: Negative

[redacted] 20[redacted] STOOL GIARDIA/CRYPTOSPORIDIUM ANTIGEN: Negative

[redacted] 20[redacted] STOOL PARASITOLOGY STAIN: Negative

Unknown date WBC: back down to normal

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
扁桃周囲膿瘍	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: PSORIASIS	19[redacted]
OTHER: STEATOSIS HEPATIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: PANCOLITIS ULCEROSA	20[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO MEFENAMIN ACID	20[redacted]
DRUG ALLERGIES/REACTIONS: PENICILLIN ALLERGY	20[redacted]
OTHER: ISCHALGIA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 367	310

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FEMODENE	1 DF (dosage form)	QD	Y-M: 20[redacted] / -321
MESALAZINE	1500 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -257
PREDNISOLONE	25 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -54
MOVIPREP	2 DF (dosage form)	QD	Y-M: 20[redacted]-[redacted] / -16
SENNA ALEXANDRINA	75 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / -16
HYOSCINE	20 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -15
PROPOFOL	480 mg (milligram(s))	QD	Y-M: 20[redacted]-[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
FEMODENE	1 DF (dosage form)	QD	Y-M: 20[redacted] / -321	ONGOING
ESCHERICHIA COLI	1 DF (dosage form)	QD	Y-M: 20[redacted]-[redacted] / 9	Y-M: 20[redacted]-[redacted] / 269
CLINDAMYCIN	600 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 228	Y-M: 20[redacted]-[redacted] / 235
DICLOFENAC	UNKNOWN mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 233	Y-M: 20[redacted]-[redacted] / 243
METAMIZOLE	25 gtt (drop(s))	PRN	Y-M: 20[redacted]-[redacted] / 233	Y-M: 20[redacted]-[redacted] / 243
CLINDAMYCIN	600 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 236	Y-M: 20[redacted]-[redacted] / 240

Event #1: Serious Adverse Event

Event Description	PERITONSILLAR ABSCESS
Preferred term	扁桃周囲膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 228
Age at AE Onset	2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 228): COMPUTED TOMOGRAPHY: PERITONSILLAR ABSCESS; [redacted]20[redacted] (RX DAY 233): TONSILLECTOMY: TONSILL AND PERITONSILLAR ABSCESS REMOVED

AE Stopped Rx Day	243
Duration of AE	16 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NO KNOWN CAUSE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（オーストリア）であり，重篤な有害事象の扁桃周囲膿瘍が認められた。関連する病歴は，乾癬，炎症性腸疾患（汎大腸炎）及び潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，扁桃周囲膿瘍が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，扁桃周囲膿瘍は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は救急治療室を受診し，咽頭痛が認められた。抗生剤の静脈内投与が行われたが，奏効は認められなかった。コンピュータ断層撮影検査の結果，扁桃周囲膿瘍が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，扁桃摘出術が実施され，膿瘍が除去された。手術は成功し，合併症はみられなかった。抗生物質療法及び疼痛治療が行われ，20[redacted] 年 [redacted] 月 [redacted] 日に被験者は良好な容体で退院した。摘出された膿瘍の組織学的検査の結果，悪性ではなかった。

治療薬としてクリンダマイシン，ジクロフェナク，及び Novalgin が投与された。

The patient's past medications include:

DALACIN for INFECTION AFTER TOOTH EXTRACTION and INFECTION AFTER TOOTH EXTRACTION ([redacted] 20[redacted] - [redacted] 20[redacted])

MEFENAMIN ACID for UNKNOWN INDICATION

PENICILLIN for UNKNOWN INDICATION

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Peritonsillar abscess (10034686) (Peritonsillar abscess (10034686)) [v.19.0] [10034686]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: No

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA40MG/0.8ML (Open Label)

Event of PERITONSILLAR ABSCESS

- Investigator: No known cause

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Computed tomography: Peritonsillar abscess

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
肋骨骨折	X			
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	5[redacted]	MALE	White

Medical History	Onset Year
OTHER: APPENDICITIS	20[redacted]
OTHER: TURBINOPLASTY	20[redacted]
SURGERY: SEPTOPLASTY	20[redacted]
OTHER: NODULI HEMORRHOIDALES GRAD III	20[redacted]
OTHER: AXIAL HIATUS HERNIA	20[redacted]
OTHER: INTOLERANCE TO AZATHIOPRIN	20[redacted]
ANEMIA: ANEMIA	20[redacted]
OTHER: URINARY TRACT INFECTION	20[redacted]
OTHER: STATUS POST CYTOMEGALOVIRUS	NOT REPORTED
OTHER: STATUS POST EPSTEIN BARR VIRUS	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	33	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 60	[redacted]20[redacted] / 361	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted] / -215
LEKOVIT CA	1 DF (dosage form)	QD	Y-M: 20[redacted]-[redacted] / -40
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -40
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / -31
METAMIZOLE	500 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / -31
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / -31
PREDNISOLONE	12.5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -27

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LEKOVIT CA	1 DF (dosage form)	QD	Y-M: 20[redacted]-[redacted] / -40	ONGOING
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / -31	ONGOING
METAMIZOLE	500 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / -31	Y-M: 20[redacted]-[redacted] / 335
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / -31	Y-M: 20[redacted]-[redacted] / 335
MESALAZINE	1000 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 60	ONGOING
METAMIZOLE	20 gtt (drop(s))	QD	Y-M: 20[redacted]-[redacted] / 336	Y-M: 20[redacted]-[redacted] / 338
PARACETAMOL	500 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 336	Y-M: 20[redacted]-[redacted] / 348
DICLOFENAC	50 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 338	Y-M: 20[redacted]-[redacted] / 338
ELECTROLYTES NOS	500 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / 339	Y-M: 20[redacted]-[redacted] / 339

METAMIZOLE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 339
NEODOLPASSE	250 mL (millilitre(s))	QD	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 339
PARACETAMOL	1 g (gram(s))	QD	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 339
UNACID	3 g (gram(s))	TID	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 342
DICLOFENAC	2 DF (dosage form)	BID	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 344
DIHYDROCODEINE	20 gtt (drop(s))	PRN	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 344
METAMIZOLE	30 gtt (drop(s))	PRN	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 344
METOCLOPRAMIDE	10 mg (milligram(s))	PRN	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 344
OTHER NUTRIENTS	3 TABLE SPOON	QD	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 344
PROBIOTICS	1 DF (dosage form)	QD	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 344
TRAMADOL	30 gtt (drop(s))	PRN	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 344
UNACID	1 DF (dosage form)	TID	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 346
METAMIZOLE	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / 345	ONGOING
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / 349	ONGOING
HYOSCINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 374	Y-M: 20[redacted] / 374
PROPOFOL	360 mg (milligram(s))	QD	Y-M: 20[redacted] / 374	Y-M: 20[redacted] / 374

Event #1: Serious Adverse Event

Event Description	FRACTURED RIBS
Preferred term	肋骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 336
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 339): CRP: 32.3 [NOT REPORTED - 0.6] MG/DL; [redacted]20[redacted] (RX DAY 342): CRP: 8.0 [NOT REPORTED - 0.6] MG/DL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 336): XRAY: BRUSED THORAX AND CERVICAL SPINE; ABDOMEN SONOGRAPHY: NO FINDINGS; [redacted]20[redacted] (RX DAY 338): RONTGEN: BRUISED THORAX AND CERVICAL SPINE; [redacted]20[redacted] (RX DAY 339): RONTGEN: NEW EFFUSION, NO PNEUMOTHORAX; [redacted]20[redacted] (RX DAY 340): COMPUTED TOMOGRAPHY: RIB FRACTURE

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	FALL FROM 3 METERS HEIGHT AT CONSTRUCTION AREA DURING WORK
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	COLITIS ULCEROSA
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 373 (12 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 374): COLONOSCOPY: NO DISEASE ACTIVITY, MAYO ENDOSCOPIC SUBSCORE 0

AE Stopped Rx Day	374 (13 DAYS AFTER LAST TREATMENT)
Duration of AE	2 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	COLITIS ULCEROSA DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（オーストリア）であり，重篤な有害事象の肋骨骨折が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，肋骨骨折が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は建設現場で仕事中に 3 m の高さから転落した。同日の晩に，胸部及び肋骨の X 線検査を受け，胸部及び頸椎の打撲と判定された。20[redacted] 年 [redacted] 月 [redacted] 日，X 線検査が再実施されたが，結果は同一であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者の全身状態は弱まり，C 反応性たん白（以下「CRP」）の測定値は高く（非重篤），原因として寛解状態であった潰瘍性大腸炎では説明がつかなかった。同日，転落の影響を明らかにするために被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，コンピュータ断層撮影検査の結果，左背部の肋骨 10 番目から 12 番目が骨折しており，肺に損傷は認められなかった。入院中に抗生剤投与による治療が行われ，CRP 値は 8.0 mg/dL に戻った。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な全身状態で退院した。肋骨骨折及び CRP 高値は継続していたが，改善した。

治療薬として Perfalgan，Neodolpasse，Elomel Isoton，Tramal（トラマドール塩酸塩），Paspertin，Voltadol，Diclobene，Novalgin，Mexalen，Unasyn（アンピシリンナトリウム／スルバクタムナトリウム），及び Paracodin が投与された。

The patient's past medications include:

AZATHIOPRIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Fractured ribs (10017307) (Rib fracture (10039117)) [v.20.1] [10017307]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of FRACTURED RIBS

- Investigator: FALL FROM 3 METERS HEIGHT AT CONSTRUCTION AREA DURING WORK

- AbbVie: EVENT IS MORE LIKELY A COMPLICATION OF TRAUMA FROM FALL AT WORK.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMEN SONOGRAPHY: NO FINDINGS

[redacted] 20[redacted] COMPUTED TOMOGRAPHY: RIB FRACTURE

[redacted] 20[redacted] CRP: 32.3 mg/dL

[redacted] 20[redacted] CRP: 8.0 mg/dL (normal <0.6)

[redacted] 20[redacted] X RAY: BRUSED THORAX AND CERVICAL SPINE

[redacted] 20[redacted] X RAY: BRUISED THORAX AND CERVICAL SPINE

[redacted] 20[redacted] X RAY: NEW EFFUSION, NO PNEUMOTHORAX
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（オーストリア）であり，重篤な有害事象の潰瘍性大腸炎が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 33 年）であり，現アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎は回復した。

肋骨骨折以後，依然として全身状態が弱まっていたため，投与 52 週時に入院して大腸内視鏡検査を実施することが決定された。兆候及び症状は潰瘍性大腸炎のものであったが，現状は寛解状態であった。20[redacted] 年 [redacted] 月 [redacted] 日，予定されていた大腸内視鏡検査のために入院した（予防措置）。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は大腸内視鏡検査の前処置薬を服用した。20[redacted] 年 [redacted] 月 [redacted] 日，大腸内視鏡検査が実施され，合併症はみられなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な全身状態で退院し，合併症は認められなかった。

被験者は既知の潰瘍性大腸炎及び大腸内視鏡検査の関連するリスク因子を有していた。

The patient's past medications include:

AZATHIOPRIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

APREDNISLON for COLITIS ULCEROSA ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BUSCAPINA for COLITIS ULCEROSA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Colitis ulcerative (10009900) (Colitis ulcerative (10009900)) [v.21.0] [10009900]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of COLITIS ULCEROSA

- Investigator: Ulcerative colitis disease.

- AbbVie: Event is more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] COLONOSCOPY: No disease activity. MAYO endoscopic subscore 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
寝汗	X			
発熱	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: APPENDECTOMY	19[redacted]
SURGERY: ABCESS LEFT BREAST	20[redacted]
SURGERY: BILATERAL TUBAL LIGATION	20[redacted]
SURGERY: CURETTAGE	20[redacted]
ANEMIA: HB 5.9G/DL	20[redacted]
OTHER: LATENT TUBERCULOSIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	20	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 64	[redacted]20[redacted] / 197	134

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
NEUROBION	1 TABLET	BID	Y-M: 20[redacted]-[redacted]
BUDESONIDE	2.3 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -221
BUDESONIDE	3 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -159
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -56
PREDNISOLONE	25 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -46
PICO-SALAX	1 SACHET	BID	Y-M: 20[redacted]-[redacted] / -36
RIFAXIMIN	400 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -35
ISONIAZID	300 mg (milligram(s))	QD	Y-M: 20[redacted]-[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
NEUROBION	1 TABLET	BID	Y-M: 20[redacted]-[redacted]	ONGOING
ISONIAZID	300 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -14	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 107	ONGOING
PREDNISOLONE	25 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 156	ONGOING

Event #1: Serious Adverse Event

Event Description	FEVER, NIGHT SWEATS
Preferred term	寝汗，発熱
AE Onset Date / Rx Day	[redacted]20[redacted] / 239 (42 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	247 (50 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	WORSENING OF UNDERLYING DISEASE IS THE MOST PROBABLE CAUSE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（オーストリア）であり，重篤な有害事象の発熱及び寝汗が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）及び潜伏結核であった。
20[redacted] 年[redacted] 月[redacted] 日，発熱及び寝汗が認められた。
被験者は入院した。20[redacted] 年[redacted] 月[redacted] 日，発熱及び寝汗は回復した。

The patient's past medications include:

ENTOCORT KLIST for ULCERATIVE COLITIS [redacted] 20[redacted] - [redacted] 20[redacted])

ENTOCORT KPS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Fever (10016558)(Pyrexia (10037660)) [v.19.0] [10016558]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

2) Night sweats (10029410) (Night sweats (10029410)) [v.19.0] [10029410]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of FEVER, NIGHT SWEATS

- Investigator: Worsening of underlying disease is the most probable cause.

- AbbVie: THE EVENT COULD BE RELATED TO REPORTED LATENT TB.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肛門性器異形成	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	5[redacted]	MALE	White

Medical History	Onset Year
MYOCARDIAL INFARCTION	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	NOT REPORTED
OTHER: EXANTHEMA WHOLE BODY	NOT REPORTED
OTHER: HYPERTENSION	NOT REPORTED
OTHER: HYPERURICEMIA	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	15	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 40	40
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 61	6

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LEKOVIT CA	1 DF (dosage form)	QD	Y-M: 20[redacted]
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	Other: EVERY 6 WEEKS	Y-M: 20[redacted]
BUDESONIDE	3 mg (milligram(s))	BID	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	100 mg (milligram(s))	QD	Y-M: 20[redacted]
ATORVASTATIN	80 mg (milligram(s))	QD	Y-M: 20[redacted]
BISOPROLOL	2.5 mg (milligram(s))	BID	Y-M: 20[redacted]
RAMIPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted]
AKTIFERRIN COMP	1 DF (dosage form)	QD	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -186
CYANOCOBALAMIN	1000 mcg (microgram(s))	QD	Y-M: 20[redacted] / -94
FUROSEMIDE	40 mg (milligram(s))	PRN	Y-M: 20[redacted] / -94
HOMEOPATHIC PREPARATION	5 gtt (drop(s))	BID	Y-M: 20[redacted] / -94
ASCORBIC ACID	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / -57
ALLOPURINOL	150 mg (milligram(s))	Other: ONCE A WEEK	Y-M: 20[redacted] / -33
BUDESONIDE	3 mg (milligram(s))	TID	Y-M: 20[redacted] / -21
TRANSIPEG	4.5 L (litre(s))	QD	Y-M: 20[redacted] / -10
LISINOPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -9

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LEKOVIT CA	1 DF (dosage form)	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	100 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
ATORVASTATIN	80 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
BISOPROLOL	2.5 mg (milligram(s))	BID	Y-M: 20[redacted]	ONGOING
RAMIPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
AKTIFERRIN COMP	1 DF (dosage form)	QD	Y-M: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -186	ONGOING
CYANOCOBALAMIN	1000 mcg (microgram(s))	QD	Y-M: 20[redacted] / -94	ONGOING
FUROSEMIDE	40 mg (milligram(s))	PRN	Y-M: 20[redacted] / -94	ONGOING

HOMEOPATHIC PREPARATION	5 gtt (drop(s))	BID	Y-M: 20[redacted] / - ONGOING 94
ASCORBIC ACID	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / - ONGOING 57
ALLOPURINOL	150 mg (milligram(s))	Other: ONCE A WEEK	Y-M: 20[redacted] / - ONGOING 33
BUDESONIDE	3 mg (milligram(s))	TID	Y-M: 20[redacted] / - Y-M: 20[redacted] / 26 21
LISINOPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -9Y-M: 20[redacted] / 28
BUDESONIDE	3 mg (milligram(s))	BID	Y-M: 20[redacted] / Y-M: 20[redacted] / 34 27
BUDESONIDE	3 mg (milligram(s))	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 40 35
THOMAPYRIN N	1 DF (dosage form)	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 52 51
SUCRALFATE	1 DF (dosage form)	PRN	Y-M: 20[redacted] / Y-M: 20[redacted] / 70 68

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

Event Description	LOW GRADE DYSPLASIA IN RECTUM
Preferred term	肛門性器異形成
AE Onset Date / Rx Day	[redacted]20[redacted] / 56
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 176): POLYPECTOMY: POLYP COMPLETELY REMOVED.

AE Stopped Rx Day	176 (115 DAYS AFTER LAST TREATMENT)
Duration of AE	121 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（オーストリア）であり，重篤な有害事象の直腸軽度異形成が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，直腸軽度異形成が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，直腸軽度異形成は回復した。
投与 8 週時の内視鏡検査時の生検で異形成が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。入院歴はなく，本事象に関連するリスク因子としては潰瘍性大腸炎が挙げられる。現在発現中の重篤な有害事象に関連する兆候及び症状はみられず，本事象に関連する家族歴は不明であった。被験者は試験を中止し，20[redacted] 年 [redacted] 月 [redacted] 日にポリープ切除術が実施され，ポリープは完全に除去された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Sucralan（スクラルファート水和物）が投与された。

The patient's past medications include:

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Anal dysplasia (10059312) (Anogenital dysplasia (10051999)) [v.19.0] [10059312]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of LOW GRADE DYSPLASIA IN RECTUM

- Investigator: Ulcerative colitis.

- AbbVie: The event is exacerbation of underlying disease of UC.

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
歩行障害	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	5[redacted]	MALE	White

Medical History	Onset Year
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE: COPD GRADE GOLD 2	NOT REPORTED
OTHER: GAIT ABNORMALITY	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1.5 PACKS	34	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 218	162

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SERETIDE	1 DF (dosage form)	BID	Y-M: 20[redacted]
TIOTROPIUM	2.5 mcg (microgram(s))	QD	Y-M: 20[redacted]
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / -197
PREDNISOLONE	75 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -82
METAMIZOLE	20 gtt (drop(s))	PRN	Y-M: 20[redacted]-[redacted] / -74
TRANSIPEG	4 L (litre(s))	QD	Y-M: 20[redacted]-[redacted] / -7
PROPOFOL	100 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / -6

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
SERETIDE	1 DF (dosage form)	BID	Y-M: 20[redacted]	ONGOING
TIOTROPIUM	2.5 mcg (microgram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / -197	ONGOING
METAMIZOLE	20 gtt (drop(s))	PRN	Y-M: 20[redacted]-[redacted] / -74	ONGOING
AMBROXOL	1 DF (dosage form)	PRN	Y-M: 20[redacted]-[redacted] / 50	Y-M: 20[redacted]-[redacted] / 69
SACCHAROMYCES BOULARDII	1 DF (dosage form)	QD	Y-M: 20[redacted]-[redacted] / 196	Y-M: 20[redacted]-[redacted] / 203
IBEROGAST	40 gtt (drop(s))	PRN	Y-M: 20[redacted]-[redacted] / 199	ONGOING

Event #1: Serious Adverse Event

Event Description	GAIT ABNORMALITIY
Preferred term	歩行障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 93
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 93): ANA: 1:640 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; ANTIBODY TITER OF DS: 33.3 [NOT REPORTED - NOT REPORTED] IU/ML; BORRELIEN SEROLOGY: POSITIV [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 94): THROAX XRAY: NO PATHOLOGICAL FINDINGS; VEP: NORMAL VEP ON BOTH SIDES; [redacted]20[redacted] (RX DAY 98): NEUROGRAPHY: NERVUS MDEIANUS RIGHT, NERVUS PERONEUS RIGHT, NERVUS TIBIALIS LEFT, NERVUS SURALIS RIGHT: ALL WITHOUT PATHOLOGICAL FINDINGS

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	AS OF YET UNKNOWN, SUSPICION OF SPASTIC PARAPARESIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（オーストリア）であり，重篤な有害事象の歩行異常が認められた。関連する病歴は，潰瘍性大腸炎及び慢性閉塞性肺疾患（グレード：GOLD 2）であった。被験者は元喫煙者（1 日当たり 1.5 箱，喫煙期間 34 年）であり，アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，歩行異常が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は歩行異常の精密診断のため入院した。入院歴聴取及び身体所見では，歩行異常の他に特筆すべき点はなかった。現時点で最終診断は得られていない。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

APREDNISLON for ULCERATIVE COLITIS [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Gait abnormal (10017573) (Gait disturbance (10017577)) [v.21.0] [10017573]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of GAIT ABNORMALITY

- Investigator: As of yet unknown, suspicion of spastic paraparesis.

- AbbVie: Event more likely related to pre-existing history of gait abnormality.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ANA: 1:640

[redacted] 20[redacted] ANTIBODY TITER OF DS: 33.3 IU/mL

[redacted] 20[redacted] BORRELIEN SEROLOGY: POSITIVE

[redacted] 20[redacted] NEUROGRAPHY: NERVUS MDEIANUS RIGHT, NERVUS PERONEUS RIGHT, NERVUS TIBIALIS LEFT, NERVUS SURALIS RIGHT: ALL WITHOUT PATHOLOGICAL FINDINGS

[redacted] 20[redacted] THROAX XRAY: NO PATHOLOGICAL FINDINGS

[redacted] 20[redacted] VISUAL EVOKED POTENTIAL: NORMAL VEP ON BOTH SIDES

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
変形性関節症	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	6[redacted]	FEMALE	White

Medical History	Onset Year
OSTEOPOROSIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 316	260

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	32 mg (milligram(s))	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	32 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted]
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]
BECLOMETASONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -188

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
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
BECLOMETASONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -188	ONGOING
PIROXICAM	20 mg (milligram(s))	PRN	Y-M: 20[redacted] / 47	ONGOING
ZOLPIDEM	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 169	ONGOING
PARACETAMOL	1000 mg (milligram(s))	TID	Y-M: 20[redacted] / 212	ONGOING
TRAMADOL	50 mg (milligram(s))	BID	Y-M: 20[redacted] / 212	Y-M: 20[redacted] / 226
MELOXICAM	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 212	Y-M: 20[redacted] / 255
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 212	Y-M: 20[redacted] / 261

Event #1: Serious Adverse Event

Event Description	BILATERAL GONARTHROSIS
Preferred term	変形性関節症
AE Onset Date / Rx Day	[redacted]20[redacted] / 212
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 212): KNEE REPLACEMENT SURGERY: FAVORABLE EVOLUTION	
AE Stopped Rx Day	215
Duration of AE	4 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	OSTEOPOROSIS

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

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の女性（ベルギー）であり，重篤な有害事象の両側変形性膝関節症が認められた。関連する病歴は，潰瘍性大腸炎及び骨粗鬆症であった。被験者は非喫煙者であり，アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，両側変形性膝関節症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，両側変形性膝関節症は回復した。

本事象の発現前には，20[redacted] 年 [redacted] 月以降に変形性膝関節症の初期段階として左膝の疼痛が認められていた。

左膝の腫大及び疼痛が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，人工左膝関節置換術が実施された。被験者はその後 2 日間入院し，20[redacted] 年 [redacted] 月 [redacted] 日に良好な容体で退院した。

治療薬としてアセトアミノフェン，メロキシカム，Pantomed，及び Tradonal Odis が投与された。

Causality for HUMIRA (Blinded)

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1) Gonarthrosis (10048794) (Osteoarthritis (10031161)) [v.20.1] [10048794]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of BILATERAL GONARTHROSIS

- Investigator: OSTEOPOROSIS

- AbbVie: RISK FACTORS INCLUDE SUBJECTS AGE AND OVERWEIGHT. ADDITIONALLY PRE-EXISTING ULCERATIVE COLITIS INCREASES THE RISK OF OSTEOARTHRITIS.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
尿閉	X			
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	2[redacted]	FEMALE	White

Medical History	Onset Year
ANEMIA: DUE TO CONDITION UNDER STUDY	20[redacted]
COGNITIVE OR PSYCHIATRIC DISORDER: ANXIETY	20[redacted]
COGNITIVE OR PSYCHIATRIC DISORDER: DEPRESSION	20[redacted]
OTHER: INSOMNIA	20[redacted]
MIGRAINE HEADACHE: HEACACHES	20[redacted]
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	20[redacted]
OTHER: HAIR LOSS	20[redacted]
KIDNEY DISORDER: PYELONEPHRITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted] / 1	[redacted] / 42	42
ADALIMUMAB TDM	40/40/160/40 MG	EOW/EW/EW/EW	[redacted] / 55	[redacted] / 217	163

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DIMENHYDRINATE	50 mg (milligram(s))	Other: AS NEEDED	Y-M: [redacted]
IRON	324 mg (milligram(s))	QD	Y-M: [redacted]
VITAMIN B12 NOS	1000 mcg (microgram(s))	QD	Y-M: [redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: [redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: [redacted]
PARACETAMOL	500 mg (milligram(s))	Other: AS NEEDED	Y-M: [redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: [redacted]
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: [redacted]
AZATHIOPRINE	200 mg (milligram(s))	QD	Y-M: [redacted]
INFLIXIMAB	400 mg (milligram(s))	Other: EVERY 2 WEEKS	Y-M: [redacted]
INFLIXIMAB	400 mg (milligram(s))	Other: EVERY 8 WEEKS	Y-M: [redacted]
INFLIXIMAB	700 mg (milligram(s))	Other: EVERY 8 WEEKS	Y-M: [redacted]
FOLIC ACID	1 mg (milligram(s))	QD	Y-M: [redacted]
METHOTREXATE	25 mg (milligram(s))	Other: EVERY WEEK	Y-M: [redacted]
METHOTREXATE	25 mg (milligram(s))	Other: EVERY 7 DAYS	Y-M: [redacted]
CALCIUM	1300 mg (milligram(s))	QD	Y-M: [redacted]
ERGOCALCIFEROL	1000 IU (international unit(s))	QD	Y-M: [redacted]
HYDROMORPHONE	4 mg (milligram(s))	Other: AS NEEDED	Y-M: [redacted]
ZOPICLONE	15 mg (milligram(s))	Other: DAILY AT BEDTIME AS NEEDED	Y-M: [redacted] / -302
TEMAZEPAM	30 - 60 mg (milligram(s))	Other: DAILY AS NEEDED	Y-M: [redacted] / -199
CENTRUM	1 TABLET	QD	Y-M: [redacted] / -163
PREDNISONE	15 mg (milligram(s))	QD	Y-M: [redacted] / -111
PREDNISONE	10 mg (milligram(s))	QD	Y-M: [redacted] / -101

PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -91
SERTRALINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -34
PREDNISONE	35 mg (milligram(s))	QD	Y-M: 20[redacted] / -24
HYDROMORPHONE	3 mg (milligram(s))	Other: AS NEEDED	Y-M: 20[redacted] / -20
PICO-SALAX	2 PACKETS	Other: ONCE ONLY	Y-M: 20[redacted] / -16
FENTANYL	200 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / -15
MIDAZOLAM	10 mg (milligram(s))	Other: ONCE	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
VITAMIN B12 NOS	1000 mcg (microgram(s))	QD	Y-M: 20[redacted]	ONGOING
IRON	324 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 108
DIMENHYDRINATE	50 mg (milligram(s))	Other: AS NEEDED	Y-M: 20[redacted]	Y-M: 20[redacted] / 281
PARACETAMOL	500 mg (milligram(s))	Other: AS NEEDED	Y-M: 20[redacted]	ONGOING
FOLIC ACID	1 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	25 mg (milligram(s))	Other: EVERY 7 DAYS	Y-M: 20[redacted]	Y-M: 20[redacted] / 219
ERGOCALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted]	ONGOING
CALCIUM	1300 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 108
HYDROMORPHONE	4 mg (milligram(s))	Other: AS NEEDED	Y-M: 20[redacted]	Y-M: 20[redacted] / 281
ZOPICLONE	15 mg (milligram(s))	Other: DAILY AT BEDTIME AS NEEDED	Y-M: 20[redacted] / -302	ONGOING
TEMAZEPAM	30 - 60 mg (milligram(s))	Other: DAILY AS NEEDED	Y-M: 20[redacted] / -199	ONGOING
CENTRUM	1 TABLET	QD	Y-M: 20[redacted] / -163	Y-M: 20[redacted] / 108
SERTRALINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -34	ONGOING

HYDROMORPHONE	3 mg (milligram(s))	Other: AS NEEDED	Y-M: 20[redacted] Y-M: 20[redacted] / / -20 219
LORAZEPAM	1 mg (milligram(s))	PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 65 95
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 72 78
PREDNISONE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 79 85
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] Y-M: 20[redacted] / / 99 109
DIMENHYDRINATE	25 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] Y-M: 20[redacted] / / 108 108
KETOROLAC	30 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] Y-M: 20[redacted] / / 108 108
VITAMINS NOS	1 TABLET	QD	Y-M: 20[redacted] ONGOING / 109
HYDROMORPHONE	2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] Y-M: 20[redacted] / / 109 109
HYDROMORPHONE	3 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] Y-M: 20[redacted] / / 109 109
METHYLPREDNISOLONE	125 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] Y-M: 20[redacted] / / 109 109
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 109 110
IRON	300 mg (milligram(s))	BID	Y-M: 20[redacted] Y-M: 20[redacted] / / 109 120
CALCIUM	650 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 109 125
CYCLOBENZAPRINE	10 mg (milligram(s))	Other: BID PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 125 128
ONDANSETRON	8 mg (milligram(s))	Other: BID PRN	Y-M: 20[redacted] Y-M: 20[redacted] / / 125 128
CALCIUM	1300 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 126 219
NITROFURANTOIN	100 mg (milligram(s))	BID	Y-M: 20[redacted] Y-M: 20[redacted] / / 128 135
LOPERAMIDE	2 mg (milligram(s))	Other: PRN-AS NEEDED	Y-M: 20[redacted] ONGOING / 136
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] Y-M: 20[redacted] / / 182 196
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] Y-M: 20[redacted] / / 182 196

DIMENHYDRINATE	25 TO 50 mg (milligram(s))	PRN	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 220
HYDROMORPHONE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 221
HYDROMORPHONE	3 mg (milligram(s))	BID	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 221
EL-4	125 ML/HOUR mL (millilitre(s))	Other: 125 ML/HOUR	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 225
HYDROMORPHONE	6 mg (milligram(s))	BID	Y-M: 20[redacted] / 221	Y-M: 20[redacted] / 222
HYDROMORPHONE	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 222	Y-M: 20[redacted] / 222
METHOTREXATE	12.5 mg (milligram(s))	Other: EVERY 7 DAYS	Y-M: 20[redacted] / 223	ONGOING
FENTANYL	100 mcg (microgram(s))	QD	Y-M: 20[redacted] / 224	Y-M: 20[redacted] / 224
MIDAZOLAM	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 224	Y-M: 20[redacted] / 224
METRONIDAZOLE	250 mg (milligram(s))	QID	Y-M: 20[redacted] / 224	Y-M: 20[redacted] / 225
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 226
METHYLPREDNISOLONE	20 mg (milligram(s))	Other: EVERY 8 HOURS	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 229
METHYLPREDNISOLONE	40 mg (milligram(s))	Other: EVERY 8 HOURS	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 233
CLONAZEPAM	1 mg (milligram(s))	BID	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 277
CLONAZEPAM	1 mg (milligram(s))	Other: PRN	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 277
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 230	Y-M: 20[redacted] / 237
FUROSEMIDE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 234
PREDNISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 251
FUROSEMIDE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 238
FENTANYL	12 mcg (microgram(s))	Other: EVERY 3 DAYS	Y-M: 20[redacted] / 239	Y-M: 20[redacted] / 245
FUROSEMIDE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 240

METHYLPREDNISOLONE	40 mg (milligram(s))	Other: EVERY 8 HOURS	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 250
FENTANYL	25 mcg (microgram(s))	Other: EVERY 3 DAYS	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 254
FUROSEMIDE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 250	Y-M: 20[redacted] / 250
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 250	Y-M: 20[redacted] / 256
NYSTATIN	500,000 UNITS	QID	Y-M: 20[redacted] / 251	Y-M: 20[redacted] / 258
FUROSEMIDE	20 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 252
CALCIUM	1200 mg (milligram(s))	QD	Y-M: 20[redacted] / 253	Y-M: 20[redacted] / 273
RANITIDINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / 255	Y-M: 20[redacted] / 277
FENTANYL	37 mcg (microgram(s))	Other: EVERY 3 DAYS	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 259
PREDNISONE	35 mg (milligram(s))	QD	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 263
DALTEPARIN	5000 UNITS	QD	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 269
ZINC	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 258	Y-M: 20[redacted] / 276
FENTANYL	12-25 mcg (microgram(s))	Other: EVERY 3 DAYS	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 268
FENTANYL	25 mcg (microgram(s))	Other: EVERY 3 DAYS	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 271
FLUCONAZOLE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 271
CEFTRIAXONE	1 g (gram(s))	Other: EVERY 24 HOURS	Y-M: 20[redacted] / 262	Y-M: 20[redacted] / 271
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 264	Y-M: 20[redacted] / 271
POTASSIUM	25 mcg (microgram(s))	QD	Y-M: 20[redacted] / 268	Y-M: 20[redacted] / 269
HYDROMORPHONE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / 269	Y-M: 20[redacted] / 278
POTASSIUM	2 TABLETS	BID	Y-M: 20[redacted] / 269	Y-M: 20[redacted] / 281
FENTANYL	62 mcg (microgram(s))	Other: EVERY 3 DAYS	Y-M: 20[redacted] / 270	Y-M: 20[redacted] / 278

PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 272 276
CALCIUM	500 mg (milligram(s))	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 273 276

Event #1: Serious Adverse Event

Event Description	URINARY RETENTION
Preferred term	尿閉
AE Onset Date / Rx Day	[redacted]20[redacted] / 108
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 109): INSERTION OF URETHRAL CATHETER: CATHETER REMOVED [redacted], 20[redacted]	
AE Stopped Rx Day	128
Duration of AE	21 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	WORSENING ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 220 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 219): EKG: NORMAL SINUS RHYTHM; [redacted]20[redacted] (RX DAY 220): ABDOMINAL XRAY, MULTIPLE VIEWS UP TO 3: NORMAL	
AE Stopped Rx Day	278 (61 DAYS AFTER LAST TREATMENT)
Duration of AE	59 DAYS

Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	WORSENING DISEASE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（カナダ）であり，重篤な有害事象の尿閉が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）及び腎盂腎炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，尿閉が認められた。被験者は腹痛，背部痛，側腹部痛，及び排尿困難を訴えた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日の入院中に，尿道留置カテーテルが挿入された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，カテーテルが除去された。20[redacted] 年 [redacted] 月 [redacted] 日，尿閉は回復した。

治療薬として Hydromorph Contin（ヒドロモルフォン塩酸塩），Gravol（ジメンヒドリナート），ヒドロモルフォン，及び Toradol が投与された。

Causality for HUMIRA (Open Label)

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1) Urinary retention (10046555) (Urinary retention (10046555)) [v.18.0] [10046555]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of URINARY RETENTION

- Investigator: N/A

- AbbVie: N/A

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（カナダ）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。
潰瘍性大腸炎の投薬による管理は不良であった。20[redacted] 年 [redacted] 月 [redacted] 日，症状及び疼痛が悪化したため，被験者は救急治療室を受診したが，入院には至らなかった。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の症状悪化のため，被験者は入院し，静脈内輸液，静脈内鎮痛管理，及び抗生剤投与が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬としてカルシウム，亜鉛，フルコナゾール，セフトリアキソン，ダルテパリン，K-Lyte，Slow-K（塩化カリウム），ナイスタチン，フェンタニルパッチ剤，prednisone，クロナゼパム，メチルプレドニゾロン，シプロフロキサシン，ヒドロモルフォン，Gravol（ジメンヒドリナート），Flagyl（メトロニダゾール），及びラニチジンが投与された。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

PREDNISONE for PROPHYLACTIC FOR ULCERATIVE COLITIS and PROPHYLACTIC FOR ULCERATIVE COLITIS ([redacted])

CIPROFLOXACIN for URINARY TRACT INFECTION and INCREASED BLOODY DIARRHEA ([redacted])

ONDANSETRON for NAUSEA RELATED TO ULCERATIVE COLITIS and NAUSEA RELATED TO ULCERATIVE COLITIS ([redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING ULCERATIVE COLITIS

- Investigator: Worsening disease

- AbbVie: Patient presenting with worsening of gastrointestinal signs leading to hospitalization. Possible worsening of ulcerative colitis.

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
膝蓋骨骨折	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	5[redacted]	MALE	White

Medical History	Onset Year
OTHER: ANXIETY	19[redacted]
OTHER: BILATERAL WRIST FRACTURE SECONDARY TO MOTORCYCLE ACCIDENT	19[redacted]
SURGERY: VASECTOMY	19[redacted]
ARTHRALGIA	20[redacted]
EYE DISEASE/DISORDER: BILATERAL FUCHS DYSTROPHY OF CORNEA	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: INTERMITTENT HEARTBURN	20[redacted]
OTHER: HEADACHES	20[redacted]
SLEEP APNEA	20[redacted]
CLOTTING/BLEEDING PROBLEMS: PROTEIN C DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	40	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 358	303

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
DICYCLOVERINE	10 mg (milligram(s))	PRN	Y-M: 20[redacted]
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg (milligram(s))	QD	Y-M: 20[redacted]
METHOTREXATE	25 mg (milligram(s))	Other: WEEKLY	Y-M: 20[redacted]
METHOTREXATE	25 mg (milligram(s))	Other: WEEKLY	Y-M: 20[redacted]
CALCIUM CARBONATE	2 TABLETS	PRN	Y-M: 20[redacted]
METHOTREXATE	20 mg (milligram(s))	Other: WEEKLY	Y-M: 20[redacted]
METHOTREXATE	15 mg (milligram(s))	Other: WEEKLY	Y-M: 20[redacted]
PARACETAMOL	2 TABLETS	PRN	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	81 mg (milligram(s))	QD	Y-M: 20[redacted]
PICO-SALAX	1 PACKET	BID	Y-M: 20[redacted] / -23
FENTANYL	100 mcg (microgram(s))	QD	Y-M: 20[redacted] / -22
MIDAZOLAM	7 mg (milligram(s))	QD	Y-M: 20[redacted] / -22
CALCIUM	650 mg (milligram(s))	BID	Y-M: 20[redacted] / -21
ERGOCALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted] / -21
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted] / -21
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -21
RIVAROXABAN	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -21
SODIUM PHOSPHATE	133 mL (millilitre(s))	QD	Y-M: 20[redacted] / -8
LORAZEPAM	1 mg (milligram(s))	PRN	Y-M: 20[redacted] / -1

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / / RX Day	Stop Year-Month / RX Day
DICYCLOVERINE	10 mg (milligram(s))	PRN	Y-M: 20[redacted]	ONGOING
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted]	ONGOING
CALCIUM CARBONATE	2 TABLETS	PRN	Y-M: 20[redacted]	ONGOING
PARACETAMOL	2 TABLETS	PRN	Y-M: 20[redacted]	ONGOING
CALCIUM	650 mg (milligram(s))	BID	Y-M: 20[redacted] / - 21	ONGOING
ERGOCALCIFEROL	1000 IU (international unit(s))	QD	Y-M: 20[redacted] / - 21	ONGOING
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted] / - 21	ONGOING
LORAZEPAM	1 mg (milligram(s))	PRN	Y-M: 20[redacted] / - 1	ONGOING
ACETYLSALICYLIC ACID	81 mg (milligram(s))	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 245
CEFAZOLIN	1 g (gram(s))	QD	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 244
FENTANYL	50 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 244
HEPARIN	5000 UNITS	BID	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 244
ONDANSETRON	4 mg (milligram(s))	PRN	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 244
HYDROMORPHONE	0.5 - 1.0 mg (milligram(s))	PRN	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 245
HYDROMORPHONE	1-2 mg (milligram(s))	PRN	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 245
METOCLOPRAMIDE	10 mg (milligram(s))	PRN	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 245
MORPHINE	2.5-7.5 mg (milligram(s))	PRN	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 245
FENTANYL	12.5-25 mcg (microgram(s))	PRN	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 249
ONDANSETRON	8 mg (milligram(s))	PRN	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 249

Event #1: Serious Adverse Event

Event Description	LEFT PATELLA FRACTURE
Preferred term	膝蓋骨骨折

AE Onset Date / Rx Day	[redacted]20[redacted] / 243
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 248): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 89 [5 - NOT REPORTED] MG/L;
[redacted]20[redacted] (RX DAY 250): HEMOGLOBIN: 117 [140 - 180] G/L; RED BLOOD COUNT: 3.8 [4.4 - 5.9] X10^12/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 245): OPEN REDUCTION INTERNAL FIXATION LEFT PA: SUCCESSFUL; KNEE X-RAY: TWO K-WIRES AND A TENSION BAND SUTURE ARE SEEN TRANSFIXING THE PATELLAR FRACTURE. ALIGNMENT ON THESE IMAGES APPEARS NEAR ANATOMIC.; [redacted]20[redacted] (RX DAY 253): LEFT LEG VEIN ULTRASOUND: COLOR FLOW, COMPRESSION AND AUTMENTATION STUDIES OF THE VEINS OF THE LEFT LOWER EXTREMITY WERE PERFORMED FROM THE LEVEL OF THE COMMON FEMORAL VEIN TO THE LEVEL OF THE POPLITEAL VEIN. PORTIONS OF THE P

AE Stopped Rx Day	245
Duration of AE	3 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	FELL AND INJURED LEFT KNEE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（カナダ）であり，重篤な有害事象の左膝蓋骨骨折が認められた。関連する病歴は，二輪車事故に続発した両側手関節骨折，左側潰瘍性大腸炎，及び関節痛であった。被験者は元喫煙者（1 日当たり 0.5 箱，喫煙期間 40 年）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，左膝蓋骨骨折が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，左膝蓋骨骨折は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はスケート中に転倒し，左膝の急性疼痛及び腫大が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，X 線検査の結果，左膝蓋骨骨折が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，左膝蓋骨の観血的整復固定が完了した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてシプロフロキサシン，sennosides，Percocet，ヘパリン，Ancef（セファゾリンナトリウム），ヒドロモルフォン，オンダンセトロン，ビサコジル坐剤，フェンタニル，Tylenol regular（アセトアミノフェン），ダルテパリン，Maxeran（メトクロプラミド），及びモルヒネが投与された。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

FOLIC ACID for NUTRITIONAL SUPPLEMENT ([redacted])

METHOTREXATE for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

RIVAROXABAN for ANTICOAGULANT PROPHYLAXIS ([redacted])

Causality for HUMIRA (Open Label)

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1) Patella fracture (10034122)(Patella fracture (10034122)) [v.19.0] [10034122]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of LEFT PATELLA FRACTURE

- Investigator: Fell and injured left knee.

- AbbVie: The cause of the event is an injury of the subject.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Knee X-ray:

Two K-Wires and a tension band suture are seen transfixing the patellar fracture. Alignment on these images appears near anatomic.

[redacted] 20[redacted] knee xray: patella fracture

[redacted] 20[redacted] left leg vein ultrasound:

Color flow, compression and augmentation studies of the veins of the left lower extremity were performed from the level of the common femoral vein to the level of the popliteal vein. Portions of the posterior tibial and peroneal veins in the calf were also visualized. There is no evidence of deep venous thrombosis. No mass or fluid collection was identifies in the soft tissues.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ウイルス感染	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
HEARING DISORDER: HEARING DEFICIT	19[redacted]
OSTEOARTHRITIS: IN JAW	19[redacted]
OTHER: ENVIRONMENTAL ALLERGY	20[redacted]
OTHER: ENDOMETRIOSIS	20[redacted]
ARTHRALGIA: ANKLES, HIPS, AND WRIST	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: BURSITIS IN HIP	20[redacted]
OTHER: C-DIFF POSITIVE	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 170	114

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
IBUPROFEN	400 mg (milligram(s))	PRN	Y-M: 19[redacted]
PARACETAMOL	650 mg (milligram(s))	PRN	Y-M: 19[redacted]
GLUCOSAMINE	1000 mg (milligram(s))	QD	Y-M: 19[redacted]
MESALAZINE	1600 mg (milligram(s))	BID	Y-M: 19[redacted]
ERGOCALCIFEROL	2000 IU (international unit(s))	QD	Y-M: 20[redacted]
VITAMINS NOS	1 DF (dosage form)	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
PROBIOTICS	2 DF (dosage form)	QD	Y-M: 20[redacted]
FISH OIL	300 mg (milligram(s))	BID	Y-M: 20[redacted]
COLYTE	1 BOTTLE	Other: ONCE	Y-M: 20[redacted] / -32
FENTANYL	100 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / -31
MIDAZOLAM	5 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -31
VANCOMYCIN	125 mg (milligram(s))	QID	Y-M: 20[redacted] / -28

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
IBUPROFEN	400 mg (milligram(s))	PRN	Y-M: 19[redacted]	ONGOING
PARACETAMOL	650 mg (milligram(s))	PRN	Y-M: 19[redacted]	ONGOING
GLUCOSAMINE	1000 mg (milligram(s))	QD	Y-M: 19[redacted]	ONGOING
MESALAZINE	1600 mg (milligram(s))	BID	Y-M: 19[redacted]	ONGOING
ERGOCALCIFEROL	2000 IU (international unit(s))	QD	Y-M: 20[redacted]	ONGOING
VITAMINS NOS	1 DF (dosage form)	QD	Y-M: 20[redacted]	ONGOING
PROBIOTICS	2 DF (dosage form)	QD	Y-M: 20[redacted]	ONGOING

AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 165
FISH OIL	300 mg (milligram(s))	BID	Y-M: 20[redacted]	ONGOING
DESLORATADINE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 16	ONGOING
MOMETASONE	1 APPLICATION	QD	Y-M: 20[redacted] / 62	ONGOING
COLESTYRAMINE	4 g (gram(s))	QD	Y-M: 20[redacted] / 109	ONGOING
HYOSCINE	10 mg (milligram(s))	PRN	Y-M: 20[redacted] / 115	Y-M: 20[redacted] / 141
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 136	Y-M: 20[redacted] / 142
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 149
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 150	Y-M: 20[redacted] / 156
PREDNISONE	17.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 163
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 170
MESALAZINE	4 g (gram(s))	Other: EVERY THREE DAYS	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 167
DALTEPARIN	5000 IU/kg (IU/kilogram)	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 168
NYSTATIN	600,000 IU (international unit(s))	TID	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 170

Event #1: Serious Adverse Event

Event Description	VIRAL INFECTION
Preferred term	ウイルス感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 166
Age at AE Onset	3[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 166): ALANINE AMINO TRANSFERASE (SGPT/ALT): 121 [0 - 50] U/L; ALKALINE PHOSPHATASE: 20 [30 - 130] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 158 [0 - 40] U/L; WHITE BLOOD COUNT: 1.7 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 167): PLATELET COUNT: 127 [140 - 450] X10^9/L; UREA: 1.1 [2.5 - 8] MMOL/L; [redacted]20[redacted] (RX DAY 168): WHITE BLOOD COUNT: 2.8 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 169): ALANINE AMINO TRANSFERASE (SGPT/ALT): 74 [0 - 50] U/L; UREA: 2.6 [2.5 - 8] MMOL/L; WHITE BLOOD COUNT: 3.6 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 170): ALKALINE PHOSPHATASE: 29 [30 - 130] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 108 [0 - 40] U/L; PLATELET COUNT: 181 [140 - 450] X10^9/L; WHITE BLOOD COUNT: 5.3 [4 - 11] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 44): Urine URINE BACTERIAL CULTURE: N; [redacted]20[redacted] (RX DAY 167): Urine URINE BACTERIAL CULTURE: P-1X10E6 CFU/L GRAM POSITIVE COCCI; Blood BLOOD BACTERIAL CULTURE: N; Stool C-DIFF: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 166): CHEST ERECT PA AND LATERAL: NORMAL CHEST; ABDOMINAL X-RAY, 2 OR MORE PROJECTIONS: RADIOGRAPHICALLY UNREMARKABLE ABDOMEN; SINUS X-RAY: NO ACUTE ABNORMALITY IS SEEN; [redacted]20[redacted] (RX DAY 168): ULTRASOUND OF THE ABDOMEN: NORMAL EXAMINATION

AE Stopped Rx Day	169
Duration of AE	4 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	POSSIBLE VIRAL INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（カナダ）であり，重篤な有害事象のウイルス感染が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，ウイルス感染が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，ウイルス感染は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は体調が悪くなり，発熱／寒気及び悪心が認められ，以後 3 日間回復しなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は救急治療室を受診後に入院し，発熱，寒気，下痢の増加，悪心による食欲不振及び水分摂取量減少を訴えた。入院時には平熱であり，皮膚乾燥及び頻脈が認められ，腹部は柔軟で腸蠕動音が聴取された。また，肝機能検査値の上昇が認められ，白血球，好中球，及びリンパ球の数値は低かった。被験者の体温は入院中平熱のままであった。腹部の超音波検査，並びに胸部及び副鼻腔の X 線検査が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Fragmin（ダルテパリンナトリウム），ナイスタチン，Salofalk（メサラジン），及び prednisone が投与された。

The patient's past medications include:

VANCOMYCIN for C-DIFF ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BUSCOPAN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40mg/0.8ml (Open Label)

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1) Viral infection (10047461) (Viral infection (10047461)) [v.19.1] [10047461]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40mg/0.8ml (Open Label)

Event of VIRAL INFECTION

- Investigator: Possible viral infection.

- AbbVie: Subject afebrile on admission and throughout hospital admission. Patient had elevated liver enzymes but low WBC/neutrophils/lympyhocytes. Patient had increased diarrhea and nausea. Imaging results still pending, but chemistry and afebrile temp less reflective of infection and increased diarrhea and elevated liver enzymes more reflective of digestive or hepatic process.

Relevant Laboratory & Other Diagnostic Tests

Rectum, sigmoid and descending colon-3=severe disease (spontaneous bleeding, ulceration)

Presence of friability- yes, Subscore 3.

Rectum and sigmoid- 1 = Mild disease (erythema, decreased vascular pattern, mild friability) and descending colon and transverse colon-0 = Normal or inactive disease

Presence of friability- No, Subscore 1.

[redacted] 20[redacted] Ultrasound of the abdomen: normal examination

[redacted] 20[redacted] Abdominal x-ray: 2 or more projections: unremarkable abdomen

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	MALE	White

Medical History	Onset Year
SURGERY: TONSILECTOMY	19[redacted]
OTHER: INTERMITTENT GENERALIZED ARTHRALGIA	20[redacted]
SURGERY: HAND WAS FRACTURED, SURGERY TO REPAIR	20[redacted]
ANEMIA: IRON DEFICIENT ANEMIA	20[redacted]
OTHER: ACNE FROM PREDNISONE USE	20[redacted]
OTHER: PREVIOUS HYDRONEPHROSIS	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted]/ 1	[redacted]20[redacted]/ 41	41

ADALIMUMAB 4040 MG MG EVERY OTHER WEEK	EOW	[redacted]20[redacted] / 59	[redacted]20[redacted] / 198	140

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CALCIUM	300 mg (milligram(s))	TID	Y-M: 20[redacted] / -264
ERGOCALCIFEROL	2000 IU (international unit(s))	QD	Y-M: 20[redacted] / -264
MESALAZINE	2400 mg (milligram(s))	BID	Y-M: 20[redacted] / -264
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -264
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / -80
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / -80
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -80
VITAMINS NOS	1 DF (dosage form)	QD	Y-M: 20[redacted] / -80
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -49
COLYTE	1 DF (dosage form)	Other: ONCE	Y-M: 20[redacted] / -7
FENTANYL	100 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / -6
MIDAZOLAM	5 mg (milligram(s))	Other: OTHER	Y-M: 20[redacted] / -6

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	300 mg (milligram(s))	TID	Y-M: 20[redacted] / -264	ONGOING
ERGOCALCIFEROL	2000 IU (international unit(s))	QD	Y-M: 20[redacted] / -264	ONGOING
MESALAZINE	2400 mg (milligram(s))	BID	Y-M: 20[redacted] / -264	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -80	ONGOING
VITAMINS NOS	1 DF (dosage form)	QD	Y-M: 20[redacted] / -80	ONGOING
SULFASALAZINE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 200
SERTRALINE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 165	ONGOING
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 185

BENZACLIN TOPICAL	30 g (gram(s))	BID	Y-M: 20[redacted] / ONGOING 186
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 186 193
PREDNISONE	17.5 mg (milligram(s))	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 194 200
CIPROFLOXACIN	400 mg (milligram(s))	Other: EVERY 12 HOURS	Y-M: 20[redacted] / Y-M: 20[redacted] / 199 200
HYDROCORTISONE	100 mg (milligram(s))	Other: EVERY 8 HOURS	Y-M: 20[redacted] / Y-M: 20[redacted] / 199 200
METRONIDAZOLE	500 mg (milligram(s))	Other: EVERY 12 HOURS	Y-M: 20[redacted] / Y-M: 20[redacted] / 199 200
CIPROFLOXACIN	500 mg (milligram(s))	Other: EVERY 12 HOURS	Y-M: 20[redacted] / ONGOING 200
HYDROCORTISONE	1 APPLICATION	BID	Y-M: 20[redacted] / ONGOING 200
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / ONGOING 200
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted] / Y-M: 20[redacted] / 200 200
METHYLPREDNISOLONE	30 mg (milligram(s))	Other: EVERY 12 HOURS	Y-M: 20[redacted] / Y-M: 20[redacted] / 200 203
ENOXAPARIN	40 mg (milligram(s))	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 200 204
ADALIMUMAB	160 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / Y-M: 20[redacted] / 201 201
MAGNESIUM SULFATE	2 g (gram(s))	Other: ONCE	Y-M: 20[redacted] / Y-M: 20[redacted] / 201 201
IRON	300 mg (milligram(s))	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 201 203
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / Y-M: 20[redacted] / 201 204
MAGNESIUM	40 mg (milligram(s))	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 201 205
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / ONGOING 205

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

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 199 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 199): ESR-WESTERGREN: 32 [0 - 15] MM/H; HEMATOCRIT: 0.38 [0.41 - 0.52] FRACTION; HEMOGLOBIN: 119 [135 - 175] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 20.2 [8 - NOT REPORTED] MG/L; [redacted]20[redacted] (RX DAY 200): ALBUMIN: 34 [35 - 50] G/L; ESR-WESTERGREN: 33 [0 - 15] MM/H; HEMATOCRIT: 0.33 [0.41 - 0.52] FRACTION; HEMOGLOBIN: 102 [135 - 175] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 13.2 [8 - NOT REPORTED] MG/L; IRON: 5 [8 - 30] UMOL/L; MAGNESIUM: 0.63 [0.7 - 1] MMOL/L; PHOSPHORUS: 1.59 [0.8 - 1.45] MMOL/L; RED BLOOD COUNT: 4.1 [4.3 - 6] X10^12/L; SATURATION INDEX: 0.07 [0.15 - 0.5] NO UNITS; [redacted]20[redacted] (RX DAY 201): HEMOGLOBIN: 108 [135 - 175] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 10.2 [8 - NOT REPORTED] MG/L; WHITE BLOOD COUNT: 11.7 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 202): HEMOGLOBIN: 105 [135 - 175] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 4.7 [8 - NOT REPORTED] MG/L; RED BLOOD COUNT: 4.2 [4.3 - 6] X10^12/L; WHITE BLOOD COUNT: 19.6 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 203): WHITE BLOOD COUNT: 26 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 204): WHITE BLOOD COUNT: 24.2 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 205): HEMATOCRIT: 0.38 [0.41 - 0.52] FRACTION; HEMOGLOBIN: 118 [135 - 175] G/L; WHITE BLOOD COUNT: 15.5 [4 - 11] X10^9/L

Microbiology

(RX DAY): Stool STOOL CULTURE: N-NEGATIVE FOR AEROMONAS, CAMPYLOBACTER, EDWARDSIELLA TARDA, ESCHERICHIA COLI 0157:H7, PLESIOMONAS, SALMONELLA, SHIGELLA AND YERSINIA; Stool CLOSTRIDIUM DIFFICILE TEST: N-NEGATIVE FOR C-DIFF; Stool OVA AND PARASITE EXAMINATION: N-INTESTINAL PARASITES, CYSTS, OR OVA WERE NOT FOUND; Other NOSE/GROIN SWAB MRSA CULTURE: N

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	205 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	7 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	WORSENING OF DISEASE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（カナダ）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。被験者はその他の併用療法として，栄養補助を目的とした複合ビタミン剤 1 回分の服用量を 1 日 1 回摂取していた（20[redacted] 年 [redacted] 月～継続中）。

20[redacted] 年 [redacted] 月，被験者は潰瘍性大腸炎と診断された。本試験への参加以前には，20[redacted] 年 [redacted] 月 [redacted] 日に潰瘍性大腸炎の増悪のため入院していた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，切迫性の血液が混じった水様性軟便の排便頻度増加が認められた。本症状は，夜間下痢，疲労，及び腹部痙攣を伴っていた。C 反応性たん白（以下「CRP」）の測定値は 20 mg/dL まで上昇した。鉄量検査の結果，鉄欠乏が認められ，フェリチン値は約 100 であり，鉄量及び鉄飽和度が低下していた。肝機能検査値は正常であった。軽度の貧血がみられ，ヘモグロビン値は 119 g/L であった。同時点での白血球数は正常であった。Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム）の投与が開始され，ステロイド剤の静脈内投与に迅速な奏効を示し，夜間下痢の回復及び排便頻度の減少が認められた。鉄欠乏の治療のため，3 日間の含糖酸化鉄輸液が開始された。アダリムマブ 160 mg の導入が実施された。迅速な奏効を示し，退院までに排便が認められ，CRP は正常値に戻った。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

治療薬としてメチルプレドニゾロンコハク酸エステルナトリウム，硫酸マグネシウム，prednisone，マグネシウム，Flagyl（メトロニダゾール），含糖酸化鉄，Cortifoam（ヒドロコルチゾン酢酸エステル），Lovenox（エノキサパリンナトリウム），シプロフロキサシン，Salofalk（メサラジン），市販薬の Humira（アダリムマブ），及びヒドロコルチゾンが投与された。

The patient's past medications include:

CIPROFLOXACIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Worsening of disease

- AbbVie: The event is exacerbation of underlying UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted]20[redacted] CRP: 20.2 MG/L (normal 0 to 8)

[redacted] 20[redacted] CRP: 13.2 MG/L (normal 0 to 8)

[redacted] 20[redacted] CRP: 10.2 MG/L (normal 0 to 8)

[redacted] 20[redacted] CRP: 4.7 MG/L

[redacted] 20[redacted] CULTURE: Negative for MRSA from nose/groin swab

[redacted] 20[redacted] ESR: 32 MM/HR (normal 0 to 15)

[redacted] 20[redacted] ESR: 33 MM/HR (normal 0 to 15)

[redacted] 20[redacted] HEMATOCRIT: 0.38 % (normal 0.41 to 0.52)

[redacted] 20[redacted] HEMATOCRIT: 0.33 % (normal 0.41 to 0.52)

[redacted] 20[redacted] HEMATOCRIT: 0.38 % (normal 0.41 to 0.52)

[redacted] 20[redacted] HEMOGLOBIN: 119 G/L (normal 135 to 175)

[redacted] 20[redacted] HEMOGLOBIN: 102 G/L (normal 135 to 175)

[redacted] 20[redacted] HEMOGLOBIN: 108 G/L (normal 135 to 175)

[redacted] 20[redacted] HEMOGLOBIN: 105 G/L (normal 135 to 175)

[redacted] 20[redacted] HEMOGLOBIN: 118 G/L (normal 135 to 175)

[redacted] 20[redacted] IRON: 5 umol/L (normal 8 to 30)

[redacted] 20[redacted] IRON SATURATION INDEX: 0.07 no units (normal 0.15 to 0.50)

[redacted] 20[redacted] MAGNESIUM: 0.63 MMOL/L (normal 0.70 to 1.00)

[redacted] 20[redacted] PHOSPHORUS: 1.59 MMOL/L (normal 0.80 to 1.45)

[redacted] 20[redacted] RBC: 4.11 X10**12/L (normal 4.30 to 6.0)

[redacted] 20[redacted] RBC: 4.24 X10**12/L (normal 4.30 to 6.0)

[redacted] 20[redacted] STOOL CULTURE: Negative for Aeromonas, Campylobacter, Edwardsiella tarda, Escherichia coli 0157:H7, Plesiomonas, Salmonella, Shigella and Yersinia

[redacted] 20[redacted] STOOL CULTURE: Ova and parasite exam negative for intestinal parasites, cysts, and ova.

[redacted] 20[redacted] STOOL CULTURE: Negative for C- Diff

[redacted] 20[redacted] WBC: 11.7 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] WBC: 19.6 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] WBC: 26.0 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] WBC: 24.2 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] WBC: 15.5 X10**9/L (normal 4.0 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
ネフローゼ症候群	X	X		
血中クレアチニン増加		X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	MALE	White

Medical History	Onset Year
OTHER: FRACTURE R ARM	19[redacted]
OTHER: ALLERGY TO PENICILLIN	19[redacted]
ANEMIA: IRON DEFICIENT	20[redacted]
ARTHRALGIA: KNEES: RIGHT AND LEFT	20[redacted]
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
OTHER: SLEEP DISTURBANCE	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 60	[redacted]20[redacted] / 66	7

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CALCIUM	500 mg (milligram(s))	QD	Y-M: 20[redacted] / -282
ERGOCALCIFEROL	2000 IU (international unit(s))	QD	Y-M: 20[redacted] / -282
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -282
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -282
BISACODYL	3 TABLETS	Other: ONCE	Y-M: 20[redacted] / -19
FENTANYL	50 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / -18
FLEET	ONE APPLICATION	Other: ONCE	Y-M: 20[redacted] / -18
MIDAZOLAM	3 mg (milligram(s))	Other: ONCE	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
CALCIUM	500 mg (milligram(s))	QD	Y-M: 20[redacted] / -282	ONGOING
ERGOCALCIFEROL	2000 IU (international unit(s))	QD	Y-M: 20[redacted] / -282	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -282	ONGOING
FENTANYL	100 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
MIDAZOLAM	5 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
AMLODIPINE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 93	ONGOING

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

Event Description	NEPHROTIC SYNDROME
Preferred term	ネフローゼ症候群

AE Onset Date / Rx Day	[redacted]20[redacted] / 73 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 73): ANA SCREEN: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; ANTI-CENTROMERE B: 46 [NOT REPORTED - 120] MFU; COMPLEMENT C4: 0.59 [0.15 - 0.5] G/L; CREATININE: 171.43 [NOT REPORTED - 13] MG/MMOL; HEP B SURFACE ANTIGE: NON REACTIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; HEPATITIS B SURFACE: 0.22 [10 - NOT REPORTED] IU/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 40.6 [NOT REPORTED - 8] MG/L; TOTAL CO2: 19 [23 - 31] MMOL/L; UREA: 7.2 [2.5 - 8] MMOL/L; URINE HEMOGLOBIN: 3+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; URINE PROTEIN (DIPSTICK TEST): 2+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; URINE RBC: >50 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; WHITE BLOOD COUNT: 7.7 [4 - 11] X10^9/L; [redacted]20[redacted] (RX DAY 79): CREATININE: 126 [50 - 120] MCMOL/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 26.6 [0 - 8] MG/L; [redacted]20[redacted] (RX DAY 94): CREATININE: 96 [50 - 120] MCMOL/L; HEMATOCRIT: 0.39 [0.41 - 0.52] FRACTION; LD: 320 [100 - 225] U/L; RED BLOOD COUNT: 1 TO 5 [NOT REPORTED - NOT REPORTED] HPF; RED BLOOD COUNT: 4.3 [4.3 - 6] X10^12/L; URINE GLUCOSE: 1 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; URINE HEMOGLOBIN: 2+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 73): PROTEIN/CREATININE URIN: PROTEIN 1.44 G/L, CREATININE 8.4, PROTEIN/CREATINE 171.43 (SHOULD BE LESS THAN 13 MG/MOL); SYPHYLIS: NON REACTIVE; HEPATITIS C ANTIBODY: NON REACTIVE; BLOOD WORK: CRP =40.6MG/L, CREATININE 116UMOL/L, ESTIMATED GFR 68ML/MIN/1.73M2), RANDOM GLUCOSE 6.8MMOL/L, SODIUM 136MMOL/L, POTASSIUM 3.8, CHLORIDE MMOL/L, TOTAL CO2 19 MMOL/L, ANION GAP 11 MMOL/L, UREA 7.2M/MOL; CT RENAL COLIC: IMPRESSION: NO RENAL, UEETERIC, OR BLADDER CALCULI. NO HYDRONEPHROSIS OR HYDROURETER. 2. SUBMUCOSAL FATTY DEPOSITION WITHIN THE SIGMOID COLON IN KEETING WITH THE PATIENT'S KNOWN HISTORY OF COLITIS.; [redacted]20[redacted] (RX DAY 75): KIDNEY/URETER/BLADDER ULTRASOUND: NO RADIOPAQUE CALCULI IDENTIFIED.

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	ELEVATED CREATININE
Preferred term	血中クレアチニン増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 79 (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	94 (28 DAYS AFTER LAST TREATMENT)
Duration of AE	16 DAYS
Severity	Moderate
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]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（カナダ）であり，重篤な有害事象のネフローゼ症候群が認められた。関連する病歴は，潰瘍性大腸炎であった。被験者は非喫煙者であり，軽度のアルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，ネフローゼ症候群が認められた。

治験薬の投与開始以降，腹痛及び尿路痛が認められ，20[redacted] 年 [redacted] 月 [redacted] 日付近に増悪した。被験者は病院を受診し，継続治療及び調査のため救急治療室に転送された。肝酵素値上昇の所見が認められた（結果の報告なし）。

被験者は血尿のリスク因子を有しており，試験中に明らかとなった。治験責任医師は「酵素値上昇の所見はネフローゼ症候群と密接に関連していた」，また，酵素値上昇は重篤性の基準を満たしていなかったと述べた。

治療薬としてアムロジピンが投与された。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PENICILLIN for UNKNOWN INDICATION

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Nephrotic syndrome (10029164) (Nephrotic syndrome (10029164)) [v.21.1] [10029164]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of NEPHROTIC SYNDROME

- Investigator: Not Applicable

- AbbVie: Nephrotic syndrome is more likely related to concomitant treatment with Mesalazine.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ANA SCREEN: Negative

[redacted] 20[redacted] ANION GAP: 11 MMOL/L

[redacted] 20[redacted] C-REACTIVE PROTEIN: 40.6 MG/L (normal <8.0)

[redacted] 20[redacted] COMPLEMENT C4: 0.59 G/L (normal 0.15 to 0.50)

[redacted] 20[redacted] CREATININE: 116 umol/L

[redacted] 20[redacted] CREATININE: 171.43 mg/mmol

[redacted] 20[redacted] CREATININE: 13.16 mg/mmol

[redacted] 20[redacted] CREATININE URINE: 8.4 G/L

[redacted] 20[redacted] CT RENAL COLIC: No renal, Ueteric, or bladder calculi. no hydronephrosis or hydroureter. 2. Submucosal fatty deposition within the sigmoid colon in keeping with the patients known history of colitis.

[redacted] 20[redacted] ESTIMATED GFR: 68 mL/min/1.73m2

[redacted] 20[redacted] GLUCOSE: 6.8 MMOL/L

[redacted] 20[redacted] GLUCOSE: 1+

[redacted] 20[redacted] HCT: 0.43 L/L

[redacted] 20[redacted] HEMATOCRIT: 0.39 L/L

[redacted] 20[redacted] HEPATITIS B SURFACE: 0.22 IU/L (normal >10.00)

[redacted] 20[redacted]HEPATITIS C ANTIBODY: Non reactive

[redacted] 20[redacted] HGB: 150 G/L

[redacted] 20[redacted] INR: 1.0 No Unit

[redacted] 20[redacted] KIDNEY/URETER/BLADDER ULTRASOUND: No radiopaque calculi identified.

[redacted] 20[redacted] LD: 320 U/L (normal 100 to 225)

[redacted] 20[redacted] LYMPHOCYTE: 2.7 X10**9/L

[redacted] 20[redacted] MCHC: 352 G/L

[redacted] 20[redacted] MCV: 92 FL

[redacted] 20[redacted] MONOCYTE: 1.2 X10**9/L (normal >0.0)

[redacted] 20[redacted] PH URINE: 5 No Unit

[redacted] 20[redacted] POTASSIUM: 3.8 No Unit

[redacted] 20[redacted] PROTEIN (URINALYSIS): 2+

[redacted] 20[redacted] PROTEIN URINE: 1.44 G/L

[redacted] 20[redacted] PROTEIN/CREATINE URINE: 171.43 mg/mol (normal <13)

[redacted] 20[redacted] PTT: 29 SEC

[redacted] 20[redacted] RBC: 4.61 X10**12/L

[redacted] 20[redacted] RBC: 4.26 X10**12/L (normal 4.30 to 6.00)

[redacted] 20[redacted] RDW: 12.1 %

[redacted] 20[redacted] SODIUM: 136 MMOL/L

[redacted] 20[redacted] SPECIFIC GRAVITY: 1.011 No Unit

[redacted] 20[redacted] SYPHYLIS: Non reactive

[redacted] 20[redacted] TOTAL CO2: 19 MMOL/L (normal 23 to 31)

[redacted] 20[redacted] UREA: 7.2 MMOL/L (normal 2.5 to 8.0)

[redacted] 20[redacted] URINE HEMOGLOBIN: 3+

[redacted] 20[redacted] URINE HEMOGLOBIN: 2+ No Unit

[redacted] 20[redacted] URINE RBC: >50

[redacted] 20[redacted] URINE RBC: 1-5

[redacted] 20[redacted] WBC: 7.7 X10**9/L (normal 4.0 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
外耳蜂巣炎	X			
外耳炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	2[redacted]	MALE	White

Medical History	Onset Year
PNEUMONIA	19[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
INFLAMMATORY BOWEL DISEASE: CROHN'S PROCTITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 61	[redacted]20[redacted] / 362	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HYDROCORTISONE	60 mg (milligram(s))	PRN	Y-M: 20[redacted]
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
MERCAPTOPURINE	125 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	500 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted]
FENTANYL	100 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / -7
MIDAZOLAM	4 mg (milligram(s))	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
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 79
FENTANYL	50 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 61
MIDAZOLAM	2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 61
CEFADROXIL	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 79
CIPROFLOXACIN	4 gtt (drop(s))	BID	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 79
PIP/TAZO	3.375 mg (milligram(s))	Other: EVERY 6 HOURS	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 82
HYDROMORPHONE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 83
CIPROFLOXACIN	4 gtt (drop(s))	BID	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 92
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 92

Event #1: Serious Adverse Event

Event Description	LEFT EXTERNAL OTITIS MEDIA WITH PERIAURICULAR CELLULITIS
Preferred term	外耳蜂巣炎，外耳炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 79
Age at AE Onset	2[redacted]

Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	92
Duration of AE	14 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（カナダ）であり，重篤な有害事象の耳介前蜂巣炎を伴う左外耳炎が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，耳介前蜂巣炎を伴う左外耳炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，発熱，左耳痛，及び左耳腫大がみられ，左外耳炎と診断された。静脈内投与による抗生物質療法が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，自宅で経口投与による抗生物質療法が継続され，耳鼻咽喉科で継続治療が行われた。耳鼻咽喉科での継続治療の終了及び感染症の回復まで治験薬及び Imuran（アザチオプリン）の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，耳介前蜂巣炎を伴う左外耳炎は回復した。

治療薬として Dilaudid（ヒドロモルフォン塩酸塩），Duricef，Ciprodex，ピペラシリン／タゾバクタム，及びシプロフロキサシンが投与された。

The patient's past medications include:

CORTENEMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

PURINETHOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Otitis externa (10033072) (Otitis externa (10033072)) [v.20.0] [10033072]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

2) External ear cellulitis (10015729) (External ear cellulitis (10015729)) [v.20.0] [10015729]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of LEFT EXTERNAL OTITIS MEDIA WITH PERIAURICAL CELLULITIS

- Investigator:

- AbbVie:

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Electrocardiogram:

Abnormal - Sinus bradycardia with marked sinus arrhythmia, not clinically significant.

[redacted] 20[redacted] Flexible Sigmoidoscopy:

Showed mild disease in his rectum and sigmoid (1 = erythema, decreased vascular pattern, and mild friability), and moderate disease in his descending colon (2 = marked erythema, absent vascular pattern, friability, and erosions). Subscore 2.

[redacted] 20[redacted] Flexible Sigmoidoscopy: Normal or inactive disease; subscore 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
食道腺癌	X		X	

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	6[redacted]	MALE	White

Medical History	Onset Year
OTHER: VARICELLA	19[redacted]
OTHER: OCCASIONAL HEADACHES	19[redacted]
OTHER: SEASONAL ALLERGIES	19[redacted]
PNEUMONIA	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPERTENSION	20[redacted]
OTHER: HYPERLIPIDEMIA	20[redacted]
SURGERY: LEFT KNEE REPLACEMENT	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	28	20[redacted]
CIGARS	FORMER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 60	[redacted]20[redacted] / 358	299

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 19[redacted]
MESALAZINE	4 g (gram(s))	PRN	Y-M: 20[redacted]
MESALAZINE	500 mg (milligram(s))	QD	Y-M: 20[redacted]
HYDROCORTISONE	60 g (gram(s))	PRN	Y-M: 20[redacted]
ATORVASTATIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]
VALSARTAN	160 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -270
FLEET	133 mL (millilitre(s))	Other: X1	Y-M: 20[redacted] / -12
FENTANYL	50 mcg (microgram(s))	Other: X1	Y-M: 20[redacted] / -11
FLEET	133 mL (millilitre(s))	Other: X1	Y-M: 20[redacted] / -11
MIDAZOLAM	1 mg (milligram(s))	Other: X1	Y-M: 20[redacted] / -11

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 (milligram(s))	PRN	Y-M: 19[redacted]	ONGOING
ATORVASTATIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
VALSARTAN	160 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -270	ONGOING

Event #1: Serious Adverse Event, Death

Event Description	ESOPHAGEAL INVASIVE ADENOSQUAMOUS CARCINOMA
Preferred term	食道腺癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 410 (52 DAYS AFTER LAST TREATMENT)

Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 404): GASTROSCOPY: ESOPHAGEAL TUMOUR IDENTIFIED. BIOPSIES OBTAINED AND PATHOLOGY REPORT DATED [redacted] 20[redacted] CONFIRMS ESOPHAGEAL CARCINOMA; [redacted]20[redacted] (RX DAY 409): CT SCAN ABDOMEN AND PELVIS: GASTROESOPHAGEAL CANCER, INNUMERABLE HYPER VASCULAR HEPATIC LESIONS INVOLVING ALL LIVER SEGMENTS, EXTENSIVE LYMPHADENOPATHY TO UPPER ABDOMEN, MESENTERY AND RETRO PERITONEUM; OSTEOLYTIC LESION L1	
AE Stopped Rx Day	440 (82 DAYS AFTER LAST TREATMENT)
Duration of AE	31 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	TO FOLLOW
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING, DEATH OF SUBJECT

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（カナダ）であり，重篤な有害事象で致死性の食道浸潤性腺扁平上皮癌が認められた。関連する病歴は，胃食道逆流症及び左側潰瘍性大腸炎であった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 28 年）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，食道浸潤性腺扁平上皮癌が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死亡原因は浸潤性腺扁平上皮癌として報告された。検死解剖実施の有無は不明である。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胃内視鏡検査によりステージ IV の食道癌と診断され，20[redacted] 年 [redacted] 月

[redacted] 日に病理医により診断が確定された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は救急治療室を受診し，嘔吐及び経口摂取の減少がみられた。治療として静脈内輸液が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，嚥下障害，悪心，及び嘔吐がみられた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はステージ IV の食道癌に伴う合併症のため死亡した。
治療薬として Versed が投与された。

The patient's past medications include:

CORTIFOAM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Esophageal adenocarcinoma (10055458) (Oesophageal adenocarcinoma (10030137)) [v.20.1] [10055458]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of ESOPHAGEAL INVASIVE ADENOSQUAMOUS CARCINOMA

- Investigator: to follow

- AbbVie: Present risk factors: medical history of gastroesophageal reflux disease (since 20[redacted]), smoker of cigarettes for 28 years (1 pack per day), age and gender.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CT SCAN OF ABDOMEN AND PELVIS: Gastroesophageal cancer, Innumerable hyper vascular hepatic lesions involving all liver segments, Extensive lymphadenopathy to upper abdomen, mesentery and retro peritoneum, osteolytic lesion L1

[redacted] 20[redacted] GASTROSCOPY: Esophageal Tumour identified. Biopsies obtained and pathology report dated [redacted] 20[redacted] confirms esophageal carcinoma

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: ALLERGY TO FLUCONAZOLE	20[redacted]
OTHER: PYLONEPHRITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	12	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 106	50

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2 g (gram(s))	BID	Y-M: 20[redacted] / -210
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -59
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -30
FLEET	1 UNIT	Other: ONCE	Y-M: 20[redacted] / -3

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 109
ENOXAPARIN	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 112
PARACETAMOL	325-650 mg (milligram(s))	PRN	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 114
METHYLPREDNISOLONE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 113
CALCIUM CARBONATE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 114
ERGOCALCIFEROL	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 114
MESALAZINE	4 g (gram(s))	BID	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 114
PREDNISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 121

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

Event Description	ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 109 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 109): ESR: 35 [0 - 20] MM/HR; HEMOGLOBIN: 122 [110 - 150] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 4.9 [1 - 10] MG/L; PLATELET COUNT: 497 [130 - 400] X10^9/L; [redacted]20[redacted] (RX DAY 112): WHITE BLOOD COUNT: 10.1 [3 - 10] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 110): Stool C-DIFF: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 105): BIOPSY COLON: SHOWS ACTIVE DISEASE; COLONOSCOPY: UC FLARE;
[redacted]20[redacted] (RX DAY 109): ABDOMEN 3 VIEWS: NO EVIDENCE OF TOXIC MEGA COLON

AE Stopped Rx Day	114 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	6 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	HOSPITALIZATION DUE TO UC FLARE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（カナダ）であり，重篤な有害事象の潰瘍性大腸炎再燃が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。被験者は喫煙者（1 日当たり 0.5 箱，喫煙期間 12 年）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃が認められた。排便頻度の増加，直腸出血，及び体重減少が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，静脈内ステロイド投与の治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃は回復した。

治療薬として prednisone，エノキサパリン，Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム），Salofalk Enemas（メサラジン浣腸剤），アセトアミノフェン，ビタミン D，及び炭酸カルシウムが投与された。

The patient's past medications include:

SALOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FLEET ENEMA for BOWEL PREPARATION and ENDOSCOPY ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

FLUCONAZOLE for UNKNOWN INDICATION

Causality for HUMIRA (Open Label)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.18.1]　[10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ULCERATIVE COLITIS FLARE

- Investigator: Hospitalization due to UC flare

- AbbVie: The event is exacerbation of underlying disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] abdominal xray 3 views: no toxic mega colon

[redacted] 20[redacted] biopsy colon: active disease

[redacted] 20[redacted] C REACTIVE PROTEIN: 4.9 MG/L (normal >1.0 to <10)

[redacted] 20[redacted] C-Diff (Stool): Negative

[redacted] 20[redacted] ESR: 35 (normal 0 to 20)

[redacted] 20[redacted] HEMOGLOBIN: 122 G/L (normal 110 to 150)

[redacted] 20[redacted] PLATELET COUNT: 497 X10**9/L (normal 130 to 400)

[redacted] 20[redacted] WBC: 10.11 X10**9/L (normal 3.00 to < 10.00)

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
消化管感染	X			
大腸炎		X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	5[redacted]	MALE	White

Medical History	Onset Year
OTHER: CHOLANGITIS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	16	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 41	41
ADALIMUMAB 4040 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 197	142

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
URSODEOXYCHOLIC ACID	1 g (gram(s))	QD	Y-M: 20[redacted]
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -67
METRONIDAZOLE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -48
PREDNISOLONE	70 mg (milligram(s))	QD	Y-M: 20[redacted] / -33
STERCULIA URENS	1 DF (dosage form)	QD	Y-M: 20[redacted] / -10

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
URSODEOXYCHOLIC ACID	1 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -67	ONGOING
PANCREATIN	50000 IU (international unit(s))	TID	Y-M: 20[redacted] / 134	ONGOING
CEFTRIAXONE	1 g (gram(s))	BID	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 213
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 215	Y-M: 20[redacted] / 219
ADALIMUMAB	80 mg (milligram(s))	Other: EVERY TWO WEEKS	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 244

Event #1: Serious Adverse Event

Event Description	INTESTINAL SURINFECTION
Preferred term	消化管感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 207 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 210): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 45.6 [0 - 5] MG/L; WHITE BLOOD COUNT: 11.6 [4 - 10] X10^9/L; [redacted]20[redacted] (RX DAY 212): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 71.1 [0 - 5] MG/L

Microbiology

(RX DAY): Stool GIARDIA: N; Stool CRYPTOSPORIDIA: N; Stool CLOSTRIDIUM DIFFICILE: N

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day 229 (32 DAYS AFTER LAST TREATMENT)

Duration of AE	23 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	SUSPICION OF INTESTINAL SURINFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	PANCOLITIS
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 236 (39 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（フランス）であり，重篤な有害事象の腸管二次感染が認められた。関連する病歴は，左側潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，腸管二次感染が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，高熱，液状便，腹痛，及び体重減少（4 kg 減少）の兆候及び症状が認められた。被験者は，潰瘍性大腸炎の病歴，免疫抑制状態，及び海外渡航のリスク因子を有していた。投薬による治療が行われ，20[redacted] 年 [redacted] 月 [redacted] 日に被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，腸管二次感染は回復した。
治療薬として Flagyl（メトロニダゾール）及び Rocephin（セフトリアキソンナトリウム水和物）が投与された。

The patient's past medications include:

FLAGYL for BOWEL DISORDER and PROBABLE INTESTINAL INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

SOLUPRED for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Gastrointestinal infection (10017964) (Gastrointestinal infection (10017964)) [v.19.0] [10017964]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of INTESTINAL SURINFECTION

- Investigator: Suspicion of intestinal surinfection.

- AbbVie: The event is due to exacerbation of underlying disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Clostridium difficile: Negative

[redacted] 20[redacted] Cryptosporidia (stool): Negative

[redacted] 20[redacted] Giardia (stool): Negative

[redacted] 20[redacted] High sensitivity C-reactive protein: 45.6 MG/L (normal 0 to 5)

[redacted] 20[redacted] WBC: 11.6 X10**9/L (normal 4 to 10)

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
潰瘍性大腸炎	X			
直腸出血	X			
貧血	X			
潰瘍性大腸炎		X		
肺塞栓症	X	X		
急性腎盂腎炎		X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	4[redacted]	FEMALE	White

Medical History	Onset Year
ANEMIA: HB: 8.3 G/DL	20[redacted]
OTHER: RHINITIS	20[redacted]
OTHER: SIGNIFICANT ASTHENIA	20[redacted]
HYPERTENSION	NOT REPORTED
OTHER: HYPOKALEMIA	NOT REPORTED
OTHER: INSOMNIA	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 64	[redacted]20[redacted] / 232	169

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -261
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -117
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -117
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -86
PREDNISOLONE	70 mg (milligram(s))	QD	Y-M: 20[redacted] / -86
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -55
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -28
CANDESARTAN	4 mg (milligram(s))	QD	Y-M: 20[redacted] / -28
POTASSIUM	600 mg (milligram(s))	BID	Y-M: 20[redacted] / -28
ZOLPIDEM	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -28
DESLORATADINE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -26

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	150 mg (milligram(s))	QD	Y-M: 20[redacted] / -28	ONGOING
CANDESARTAN	4 mg (milligram(s))	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / 191
FOLIC ACID	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 9	ONGOING
POTASSIUM	600 mg (milligram(s))	QD	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 73
LOPRAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 141

CALCIUM CARBONATE	1000 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 74	ONGOING
PAPAVER SOMNIFERUM W/PARACETAMOL	500 mg (milligram(s))	TID	Y-M: 20[redacted]- [redacted] / 82	ONGOING
LITHIUM	8 % (percent)	BID	Y-M: 20[redacted]- [redacted] / 85	Y-M: 20[redacted]- [redacted] / 145
KETOCONAZOLE	2 % (percent)	QD	Y-M: 20[redacted]- [redacted] / 86	Y-M: 20[redacted]- [redacted] / 152
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 102	Y-M: 20[redacted]- [redacted] / 128
PHLOROGLUCINOL	80 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 111	ONGOING
DESONIDE	0.1 % (percent)	PRN	Y-M: 20[redacted]- [redacted] / 152	ONGOING
CORTISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 200	Y-M: 20[redacted]- [redacted] / 243
BLOOD AND RELATED PRODUCTS	NOT REPORTED	Other: ONCE	Y-M: 20[redacted]- [redacted] / 234	Y-M: 20[redacted]- [redacted] / 234
GENERAL NUTRIENTS	500 mL (millilitre(s))	QD	Y-M: 20[redacted]- [redacted] / 236	Y-M: 20[redacted]- [redacted] / 266
LEVOFLOXACIN	0.6 mL (millilitre(s))	BID	Y-M: 20[redacted]- [redacted] / 237	Y-M: 20[redacted]- [redacted] / 245
CEFTRIAXONE	1 g (gram(s))	Other: UNKNOWN	Y-M: 20[redacted]- [redacted] / 242	Y-M: 20[redacted]- [redacted] / 247
FLUINDIONE	20 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted] / 246	ONGOING
INFLIXIMAB	10 mg/kg (milligram(s)/kilogram)	Other: EVERY TWO WEEKS	Y-M: 20[redacted]- [redacted] / 247	Y-M: 20[redacted]- [redacted] / 257
AUGMENTIN	1 g (gram(s))	TID	Y-M: 20[redacted]- [redacted] / 248	Y-M: 20[redacted]- [redacted] / 255
INFLIXIMAB	10 mg/kg (milligram(s)/kilogram)	Other: EVERY 4 WEEKS	Y-M: 20[redacted]- [redacted] / 257	ONGOING

Event #1: Serious Adverse Event

Event Description	RECTAL BLEEDING DUE TO FLARE OF ULVERATIVE COLITIS DISEASE
Preferred term	潰瘍性大腸炎，直腸出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 102
Age at AE Onset	4[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 103): HEMOGLOBIN: 113 [120 - 115] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 104): RECTOSIGMOIDOSCOPY: SCORE MAYO 2

AE Stopped Rx Day	104
Duration of AE	3 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	FLARE OF ULCERATIVE COLITIS DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 234 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 234): HEMOGLOBIN: 63 [120 - 160] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 237): SIGMOIDOSCOPY: ENDOSCOPY SUBSCORE = 3; CT SCAN: DISCOVERY OF PULMONARY EMBOLISM

AE Stopped Rx Day	327 (95 DAYS AFTER LAST TREATMENT)
Duration of AE	94 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	FLARE OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 234 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 237): HEMOGLOBIN: 96 [120 - 160] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 36.8 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 237): SIGMOIDOSCOPY: ENDOSCOPY SUBSCORE = 3

AE Stopped Rx Day	257 (25 DAYS AFTER LAST TREATMENT)
Duration of AE	24 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UC PROGRESSION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 237 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 248): HEMOSTASE: 1.6 [2 - 3] UNITS

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 237): ABDOMINAL AND PELVIC CT: PULMONARY EMBOLISM

AE Stopped Rx Day	248 (16 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	FAMILY HISTORY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #5: AE Leading to Discontinuation of Study Drug

Event Description	ACUTE PYELONEPHRITIS
Preferred term	急性腎盂腎炎

AE Onset Date / Rx Day	[redacted]20[redacted] / 242 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	257 (25 DAYS AFTER LAST TREATMENT)
Duration of AE	16 DAYS
Severity	Moderate
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]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（フランス）であり，重篤な有害事象の潰瘍性大腸炎再燃による直腸出血が認められた。関連する病歴は，左側潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃による直腸出血が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。著しい無力症及び血便を含む兆候及び症状が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃による直腸出血は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Solupred が投与された。

The patient's past medications include:

SOLUPRED for ULCERATIVE COLITIS and FLARE OF ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PENTASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

LITHIODERM for SKIN RASH ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.19.1]　[10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2)　Rectal bleeding (10038035)　(Rectal haemorrhage (10038063))　[v.19.1]　[10038035]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA(Open Label)

Event of RECTAL BLEEDING DUE TO FLARE OF ULCERATIVE COLITIS DISEASE

- Investigator: Flare of ulcerative colitis disease

- AbbVie: Exacerbation of underlying disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Hemoglobin: 11.3 G/DL (normal 12 to 11.5)

[redacted] 20[redacted] Rectosigmoidoscopy: Score mayo 2
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（フランス）であり，重篤な有害事象の貧血，潰瘍性大腸炎再燃，及び肺塞栓症が認められた。関連する病歴は，左側潰瘍性大腸炎及び高血圧であった。
20[redacted] 年 [redacted] 月 [redacted] 日，貧血が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，肺塞栓症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，肺塞栓症は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎再燃は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。これらの事象に対して，ヘモグロビン値 6.9 g/dL，直腸出血，及び無力症を含む兆候及び症状が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Previscan，Modulen IBD，Augmentin（クラブラン酸カリウム／アモキシシリン水和物），Lovenox（エノキサパリンナトリウム），Inflectra（インフリキシマブ），Izalgi，輸血，及び Rocephin（セフトリアキソンナトリウム水和物）が投与された。

The patient's past medications include:

SOLUPRED for FLARE OF ULCERATIVE COLITIS DISEASE and ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PENTASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1)　Anemia (10002272)　(Anaemia (10002034))　[v.21.1]　[10002272]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.21.1]　[10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

3)　Pulmonary embolism (10037377)　(Pulmonary embolism (10037377))　[v.21.1]　[10037377]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of ANEMIA

- Investigator: N/A

- AbbVie: The subject presented with low RBC at Screening visit, prior to the study drug initiation.

Event of FLARE OF ULCERATIVE COLITIS

- Investigator: UC progression

- AbbVie: THE EVENT IS EXACERBATION OF UNDERLYING UC.

Event of PULMONARY EMBOLISM

- Investigator: Family history

- AbbVie: The event is more likely related to pre-existing ulcerative colitis and family history per PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Abdominopelvic CT: Pulmonary embolism

[redacted] 20[redacted] CT SCAN: Discovery of pulmonary embolism

[redacted] 20[redacted] Hemoglobin: 6.3 G/DL (normal 12.0 to 16.0)

[redacted] 20[redacted] Hemoglobin: 9.6 G/DL (normal 12.0 to 16.0)

[redacted] 20[redacted] SIGMOIDOSCOPY: Endoscopy subscore =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
糖尿病	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	5[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: OBESITY IN CHILDHOOD	19[redacted]
OTHER: PENICILLIN ALLERGY	19[redacted]
OTHER: ARTHROSIS	20[redacted]
MIGRAINE HEADACHE	20[redacted]
OTHER: CODEIN ALLERGY	20[redacted]
UVEITIS	20[redacted]
HYPERTENSION	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	UNKNOWN			
CIGARETTES	FORMER	1.5 PACKS	39	20[redacted]
CIGARS	UNKNOWN			
PIPES	UNKNOWN			

Alcohol Use	Status	Number/Day
ALCOHOL	UNKNOWN	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42

ADALIMUMAB 40 MG 40 MG EVERY OTHER WEEK	EOW	[redacted]20[redacted] / 56 [redacted]20[redacted] / 210		155

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	10 mg/kg (milligram(s)/kilogram)	Other: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted] / -230
MESALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted]-[redacted] / -111
MESALAZINE	1 ONE TIME	QD	Y-M: 20[redacted]-[redacted] / -110
PREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -99
ATROPINE	UNK gtt (drop(s))	QD	Y-M: 20[redacted]-[redacted] / -22
DEXAMETHASONE	UNK gtt (drop(s))	QD	Y-M: 20[redacted]-[redacted] / -22
STER-DEX	UNK mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -22
CO-DIOVAN	160 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -19
PREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -19
SPASFON	60 mg (milligram(s))	Other: 6 PER DAY	Y-M: 20[redacted]-[redacted] / -19

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
CO-DIOVAN	160 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -19	ONGOING
PREDNISOLONE	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 115	Y-M: 20[redacted]-[redacted] / 127
PARACETAMOL	1 g (gram(s))	Other: AS NEEDED	Y-M: 20[redacted]-[redacted] / 154	ONGOING
SPASFON	160 mg (milligram(s))	Other: AS NEEDED	Y-M: 20[redacted]-[redacted] / 154	ONGOING
DAIVOBET	50 MCG / 0.5 MG / G POMADE	QD	Y-M: 20[redacted]-[redacted] / 154	Y-M: 20[redacted]-[redacted] / 168
ROSUVASTATIN	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 157	ONGOING

SITAGLIPTIN	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 157	ONGOING
POTASSIUM	600 mg (milligram(s))	BID	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 227
GLICLAZIDE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 158	Y-M: 20[redacted] / 197

Event #1: Serious Adverse Event

Event Description	DISCOVERY OF DIABETES
Preferred term	糖尿病
AE Onset Date / Rx Day	[redacted]20[redacted] / 156
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 157): HDL CHOLESTEROL: 0.83 [0 - 1.03] MMOL/L; HEMOGLOBIN: 11.9 [12 - NOT REPORTED] G/DL; LDL CHOLESTEROL: 3.57 [0 - 2.59] MMOL/L; TRIGLYCERIDES: 3.98 [0 - 1.7] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 157): ECG: NORMAL

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の女性（フランス）であり，重篤な有害事象の糖尿病が認められた。関連する病歴は，中等度から重度の活動性潰瘍性大腸炎（全大腸炎型），ぶどう膜炎，及び高血圧であった。

20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な視力低下が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，糖尿病が認められた。後日，糖尿病は回復した（年月日不明）。多飲を伴わない多尿症候群が認められ，1 ヵ月のうちに体重が 1 kg 減少した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。糖尿病は治療により管理されていた。20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な高コレステロール血症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Crestor（ロスバスタチンカルシウム）及び Januvia（シタグリプチンリン酸塩水和物）が投与された。

The patient's past medications include:

PENICILLIN for UNKNOWN INDICATION (Started 19[redacted])

CODEIN for UNKNOWN INDICATION (Started 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PENTASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

SOLUPRED for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ATROPINE for UVEITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DEXAFREE for UVEITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

STERDEX for UVEITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COSOPT for UVEITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CELESTENE for UVEITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1)　Diabetes (10012594)　(Diabetes mellitus (10012601))　[v.21.0]　[10012594]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of DISCOVERY OF DIABETES

- Investigator: Unknown

- AbbVie: Based on currently available limited information, it could be preexisting event.

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	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	2[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: ANEMIA	20[redacted]
MIGRAINE HEADACHE	NOT REPORTED
OTHER: ATOPIC DERMATITIS	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0 PACKS	15	20[redacted]
CIGARS	FORMER			
E-CIGARETTES	NEVER			
PIPES	FORMER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42

ADALIMUMAB 4040 MG MG EVERY OTHER WEEK	EOW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 307	252

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -137
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]-[redacted] / -89

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ERYTHROMYCIN	4 % (percent)	QD	Y-M: 20[redacted]-[redacted] / 80	ONGOING
OXAZEPAM	10 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 313	ONGOING
SPASFON	40 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 313	ONGOING
METHYLPREDNISOLONE	60 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 313	Y-M: 20[redacted]-[redacted] / 317
ENOXAPARIN	4000 UI	BID	Y-M: 20[redacted]-[redacted] / 313	Y-M: 20[redacted]-[redacted] / 319
METRONIDAZOLE	500 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 313	Y-M: 20[redacted]-[redacted] / 319
OFLOXACIN	200 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 313	Y-M: 20[redacted]-[redacted] / 319
METHYLPREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 317	ONGOING
CICLOSPORIN	2 mg/kg (milligram(s)/kilogram)	QD	Y-M: 20[redacted]-[redacted] / 317	Y-M: 20[redacted]-[redacted] / 317
INFLIXIMAB	5 mg/kg (milligram(s)/kilogram)	Other: EVERY 4 WEEK	Y-M: 20[redacted]-[redacted] / 318	ONGOING

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

Event Description	SEVERE ACUTE COLITIS
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 312 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 312): HEMOGLOBIN: 148 [120 - 160] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 68 [0 - 10] MG/L; PLATELET COUNT: 316 [150 - 450] X10^9/L; WHITE BLOOD COUNT: 6.8 [4 - 10] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 283): Blood CYTOMEGALOVIRUS: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 312): ABDOMINAL AND PELVIC CT SCAN: PANCOLITIS

AE Stopped Rx Day	319 (12 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	FLARE OF ULCERATIVE COLITIS DISEASE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（フランス）であり，重篤な有害事象の重度の急性大腸炎が認められた。関連する病歴は，潰瘍性大腸炎及び貧血であった。被験者は元喫煙者（喫煙期間 15 年）であり，元アルコール摂取者（1 日当たり 2 ドリンク未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，重度の急性大腸炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，重度の急性大腸炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，入院時点で 1 週間の下痢が続いており，排便回数は 1 日当たり 10 回で血液及び粘液は含まれず，夜間中途覚醒を伴っていた。排便前に腹痛，それ以外では腹部不快感が認められた。また，被験者から直近に心窩部灼熱感がみられたとの報告があった。38.5°C の発熱エピソードが 1 回認められたが，その後の再発はみられなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Spasfon，Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム），シプロフロキサシン，及び Seresta が投与された。

The patient's past medications include:

SOLUPRED for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PENTASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of SEVERE ACUTE COLITIS

- Investigator: Flare of ulcerative colitis disease

- AbbVie: Event is more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL AND PELVIC CT SCAN: uncomplicated recto-pancolite

[redacted] 20[redacted] HEMOGLOBIN: 14.8 G/DL (normal 12 to 16)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 68 MG/L (normal 0 to 10)

[redacted] 20[redacted] NEUTROPHILS: 4660 /mm3 (normal 1500 to 7000)

[redacted] 20[redacted] PLATELET COUNT: 316 X10**9/L (normal 150 to 450)

[redacted] 20[redacted] TEMPERATURE: 38.5 Degrees C

[redacted] 20[redacted] WBC: 6760 /mm3 (normal 4000 to 10000)

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
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: MENISCUS OPERATION	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	UNKNOWN	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 55	[redacted]20[redacted] / 55	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	125 mg (milligram(s))	QD	Y-M: 20[redacted]
ADALIMUMAB	160 mg (milligram(s))	Other: ALL 14 DAYS	Y-M: 20[redacted]
PREDNISONE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
INFLIXIMAB	300 mg (milligram(s))	PRN	Y-M: 20[redacted]
BUDESONIDE	56 mg (milligram(s))	BID	Y-M: 20[redacted]
MOVIPREP	2 L (litre(s))	QD	Y-M: 20[redacted] / -15
MIDAZOLAM	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
PROPOFOL	50 mg (milligram(s))	QD	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
MIDAZOLAM	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 55
PROPOFOL	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 55

Event #1: Serious Adverse Event

Event Description	WORSING OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 82 (27 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 83): LAPAROSCOPICALLY ASSISTED COLECTOMY: COLECTOMY WAS SUCCESSFUL, PATIENT WAS DISCHARGED IN GOOD CONDITION AFTER SURGERY

AE Stopped Rx Day	90 (35 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NO INFORMATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（ドイツ）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。炎症の増加及び排便頻度の増加（Mayo スコア 3）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化のために事前に予定されていた腹腔鏡下結腸切除術のため入院し，20[redacted] 年 [redacted] 月 [redacted] 日に手術は終了した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は術後良好な容体で退院し，外来での治療が継続された。

The patient's past medications include:

AZATHIOPRIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DECORTIN for ULCERATIVE COLITIS (Started [redacted] 20[redacted], Stopped [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BUDENOFALK for ULCERATIVE COLITIS (Started [redacted] 20[redacted], Stopped [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF UC

- Investigator: NO INFORMATION

- AbbVie: The event is due to exacerbation of underlying disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Rectum - 2 = moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Sigmoid - 3 = severe disease (spontaneous bleeding, ulceration)

Descending colon - 1 = mild disease (erythema, decreased vascular pattern, mild friability)

Transverse colon - 1 = mild disease (erythema, decreased vascular pattern, mild friability)

Ascending colon/cecum - 1 = mild disease (erythema, decreased vascular pattern, mild friability)

Presence of friability? Yes

Subscore 3

[redacted] 20[redacted] Colonoscopy:

Rectum - 3 = severe disease (spontaneous bleeding, ulceration)

Sigmoid - 3 = severe disease (spontaneous bleeding, ulceration)

Descending colon - severe disease (spontaneous bleeding, ulceration)

Transverse colon - 1 = mild disease (erythema, decreased vascular pattern, mild friability)

Ascending colon/cecum - 0 = Normal or inactive disease

Presence of friability? No

Subscore 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
肺炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	3[redacted]	MALE	White

Medical History	Onset Year
OTHER: IRON DEFICIENCY ANEMIA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 261	204

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	175 mg (milligram(s))	QD	Y-M: 20[redacted] / -341
PREDNISOLONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -19
MOVIPREP	2 L (litre(s))	QD	Y-M: 20[redacted] / -13
MIDAZOLAM	2.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -12
PROPOFOL	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -12

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	175 mg (milligram(s))	QD	Y-M: 20[redacted] / -341	Y-M: 20[redacted] / 228
PREDNISOLONE	80 mg (milligram(s))	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 113
LEKOVIT CA	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 113	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 113	ONGOING
PREDNISOLONE	70 mg (milligram(s))	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 121
PREDNISOLONE	60 mg (milligram(s))	QD	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 127
PREDNISOLONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 134
CEFUROXIME	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 131
CLARITHROMYCIN	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 131
CEFUROXIME	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 132	Y-M: 20[redacted] / 141
CLARITHROMYCIN	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 132	Y-M: 20[redacted] / 141

Event #1: Serious Adverse Event

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 131

Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 131): X-RAY: RIGHT MIDDLE LOBE INFILTRATE	
AE Stopped Rx Day	132
Duration of AE	2 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NO
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ドイツ）であり，重篤な有害事象の肺炎が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。被験者は非喫煙者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，肺炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎のため入院した。被験者は風邪の症状のため病院を受診した。抗生剤投与による治療が行われ，症状は改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてセフロキシム及びクラリスロマイシンが投与された。

Causality for HUMIRA (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.20.0] [10035664]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of PNEUMONIA

- Investigator: No

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] X-RAY: RIGHT MIDDLE LOBE INFILTRATE

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
橈骨骨折	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	3[redacted]	FEMALE	White

Medical History	Onset Year
Not reported.	

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACKS	12	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
EUGYNON	1 TABLET	QD	Y-M: 19[redacted]
MESALAZINE	3 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted]
METAMIZOLE	38 DROPS	PRN	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	5 MG PER KG BODY WEIGHT	Other: EVERY 4 WEEKS	Y-M: 20[redacted]-[redacted] / -267
PREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -83
MIDAZOLAM	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -20
PROPOFOL	80 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -20
TRAVAD PHOSPHATE	120 mL (millilitre(s))	QD	Y-M: 20[redacted]-[redacted] / -20

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
EUGYNON	1 TABLET	QD	Y-M: 19[redacted]	ONGOING
MESALAZINE	3 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted]	ONGOING
METAMIZOLE	38 DROPS	PRN	Y-M: 20[redacted]-[redacted]	ONGOING
MIDAZOLAM	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 57	Y-M: 20[redacted]-[redacted] / 57
PROPOFOL	80 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 57	Y-M: 20[redacted]-[redacted] / 57
METAMIZOLE	38 DROPS	PRN	Y-M: 20[redacted]-[redacted] / 82	Y-M: 20[redacted]-[redacted] / 152

Event #1: Serious Adverse Event

Event Description	LEFT DISTAL RADIUS FRACTURE
Preferred term	橈骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 82
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 82): OPEN REPOSITION, PALMARE OSTEOSYNTHESIS: SUCCESSFULL SURGERY	
AE Stopped Rx Day	152
Duration of AE	71 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NO

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

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（ドイツ）であり，重篤な有害事象の左橈骨遠位端骨折が認められた。関連する病歴は，左側潰瘍性大腸炎であった。被験者は元喫煙者（1 日当たり 0.5 箱，喫煙期間 12 年）であった。
20[redacted] 年 [redacted] 月 [redacted] 日，左橈骨遠位端骨折が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，左橈骨遠位端骨折は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左橈骨遠位端骨折のため入院し，左橈骨遠位端の疼痛を訴えた。手術が実施され，観血的整復術及び手掌の骨接合術が同日に行われた。手術は成功し，20[redacted] 年 [redacted] 月 [redacted] 日に被験者は退院した。
治療薬として Novalgin が投与された。

The patient's past medications include:

PREDNISOLON for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Radius fracture (10037802) (Radius fracture (10037802)) [v.22.0] [10037802]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of LEFT DISTAL RADIUS FRACTURE

- Investigator: Not reported.

- AbbVie: The event is not related to underlying disease but could be a result of an accident.

Subject [redacted](Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
上肢骨折	X			
肺塞栓症	X	X	X	

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	6[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: MENOPAUSA	19[redacted]
ASTHMA	NOT REPORTED
EYE DISEASE/DISORDER	NOT REPORTED
GASTROESOPHAGEAL REFLUX DISEASE	NOT REPORTED
HYPERTENSION	NOT REPORTED
OSTEOPOROSIS	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 95	39

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DUOVENT	1 DF (dosage form)	Other: PRN	Y-M: 20[redacted]
CALCIUM	200 mg (milligram(s))	QD	Y-M: 20[redacted]
FAMOTIDINE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
AMLODIPINE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]
VALSARTAN	80/125 mg (milligram(s))	QD	Y-M: 20[redacted]
IBANDRONIC ACID	3 mg (milligram(s))	PRN	Y-M: 20[redacted]
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / -81
PICO-SALAX	1 DF (dosage form)	PRN	Y-M: 20[redacted] / -6
ATROPINE	0.5 mg (milligram(s))	QD	Y-M: 20[redacted] / -5
MIDAZOLAM	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -5
PETHIDINE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -5

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
DUOVENT	1 DF (dosage form)	Other: PRN	Y-M: 20[redacted]	ONGOING
CALCIUM	200 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
FAMOTIDINE	40 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
AMLODIPINE	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
VALSARTAN	80/125 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
IBANDRONIC ACID	3 mg (milligram(s))	PRN	Y-M: 20[redacted]	ONGOING
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / -81	Y-M: 20[redacted] / 87
NIFLUMIC ACID	500 mg (milligram(s))	PRN	Y-M: 20[redacted] / 60	ONGOING
AUGMENTIN	1.2 g (gram(s))	TID	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 63

Event #1: Serious Adverse Event

Event Description	RIGHT SHOULDER FRACTURE
Preferred term	上肢骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 60
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 61): SURGERY RIGHT SHOULDER: RESOLVED	
AE Stopped Rx Day	61
Duration of AE	2 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ACCIDENT ONLY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY

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

Event Description	EMBOLIA PULMONUM
Preferred term	肺塞栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 92
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	97 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	6 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative	POSSIBLE ALTERNATIVE ETIOLOGY FOR THE FATAL EVENT :RIGHT SHOULDER

Etiology	FRACTURE BUT NO AVAILABLE DOCUMENTATION/INFORMATION OF THE ETIOLOGY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING, DEATH OF SUBJECT

Generated: [redacted] 20[redacted]:02:12
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，7[redacted] 歳の女性（ハンガリー）であり，重篤な有害事象の右肩骨折が認められた。関連する病歴は，骨粗鬆症であった。

20[redacted] 年 [redacted] 月 [redacted] 日，右肩骨折が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，右肩骨折は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は転倒し，右肩を骨折した。右肩の運動による疼痛，並びに右肩及び前腕中央部のびまん性紅潮が認められ，その他の兆候及び症状はみられなかった。冷却及び包帯固定による保存療法を行ったが，患者の訴える症状は回復しなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，右肩の手術が実施された。麻酔剤及び抗生剤が投与された。合併症は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Augmentin（クラブラン酸カリウム／アモキシシリン水和物）及び Donalgin が投与された。

Causality for HUMIRA (Open Label)

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1) Shoulder fracture (10049128) (Upper limb fracture (10061394)) [v.19.0] [10049128]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of RIGHT SHOULDER FRACTURE

- Investigator: Accident only.

- AbbVie: THE EVENT IS NOT RELATED TO STUDY DRUG TREATMENT. THE SUBJECT HAS KNOWN MEDICAL HISTORY OF OSTEOPOROSIS.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，7[redacted] 歳の女性（ハンガリー）であり，重篤な有害事象で致死性の肺塞栓症が認められた。関連する病歴は，閉経，左側潰瘍性大腸炎，高血圧，骨粗鬆症，及び喘息であった。
20[redacted] 年 [redacted] 月 [redacted] 日，肺塞栓症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死亡原因は肺塞栓症として報告された。検死解剖実施の有無は不明である。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は呼吸困難のため入院した。本事象，入院，及び治療についての詳細は得られなかった。リスク因子として 20[redacted] 年 [redacted] 月に発現した肩骨折の報告があった。
治療薬として Augmentin（クラブラン酸カリウム／アモキシシリン水和物）及び Donalgin が投与された。

Causality for HUMIRA (Open Label)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.20.0] [10037377]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of PULMONARY EMBOLI

- Investigator: Right shoulder fracture

- AbbVie: THE EVENT MIGHT BE RELATED TO KNOWN MEDICAL HISTORY OF ASTHMA AND HYPERTENSION

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
鼻中隔弯曲	X			
角層下膿疱性皮膚症	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	6[redacted]	FEMALE	White

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: UC DIAGNOSIS	19[redacted]
OTHER: MENOPAUSE	20[redacted]
SURGERY: BILATERAL LAPEROSCOPIC SALPINGOOVARECTOMY	20[redacted]
SURGERY: EYEBROW ELEVATION	20[redacted]
OTHER: HYPERCHOLESTEROLEMIA	20[redacted]
OTHER: HIATAL HERNIA	20[redacted]
OTHER: DEVIATED NASAL SEPTUM	20[redacted]
OTHER: POSITIVE TB TEST	20[redacted]
OTHER: BACK DISCOMFORT	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 148	93

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2 g (gram(s))	TID	Y-M: 19[redacted]
PREDNISONE	40 mg (milligram(s))	UNKNOWN	Y-M: 20[redacted]
RIFAMPICIN	300 mg (milligram(s))	BID	Y-M: 20[redacted] / -124
FENTANYL	50 mcg (microgram(s))	QD	Y-M: 20[redacted] / -43
FLEET	2 BOTTLE	BID	Y-M: 20[redacted] / -43
MIDAZOLAM	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -43
PARACETAMOL	500 g (gram(s))	Other: ONCE	Y-M: 20[redacted] / -12

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
MESALAZINE	2 g (gram(s))	TID	Y-M: 19[redacted]	ONGOING
SIMVASTATIN	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 8	Y-M: 20[redacted] / 77
ATORVASTATIN	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 161
METAMIZOLE	1 g (gram(s))	QD	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 100
PARACETAMOL	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 101
CLOBETASOL	25 mg (milligram(s))	BID	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 133
PERMETHRIN	5 % (percent)	BID	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 133
COAL TAR	5 % (percent)	PRN	Y-M: 20[redacted] / 153	ONGOING

ALL OTHER NON-THERAPEUTIC PRODUCTS	NA NA	Other: ONE WEEK, TOTAL*4	Y-M: 20[redacted] / Y-M: 20[redacted] / 153 161
HYDROCORTISONE	2 % (percent)	PRN	Y-M: 20[redacted] / Y-M: 20[redacted] / 153 185
FENTANYL	50 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / Y-M: 20[redacted] / 161 161
MIDAZOLAM	3 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / Y-M: 20[redacted] / 161 161

Event #1: Serious Adverse Event

Event Description	DEVIATED NASAL SEPTUM
Preferred term	鼻中隔弯曲
AE Onset Date / Rx Day	[redacted]20[redacted] / 100
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 100): SUB MUCOUS RESECTION +TUBINECTOMY BY DIA: NASAL ABSTRUCTION RESOVLED	
AE Stopped Rx Day	102
Duration of AE	3 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ELECTIVE SURGERY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	SUBCORNEAL PUSTULAR DERMATOSIS
Preferred term	角層下膿疱性皮膚症
AE Onset Date / Rx Day	[redacted]20[redacted] / 113
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	

SAE Supplemental Procedure

(RX DAY): SIGMOIDOSCOPY: UC; [redacted]20[redacted] (RX DAY 154): SKIN BIOPSY: SUPERFICIAL AND DEEP PURULENT FOLLICULITIS; [redacted]20[redacted] (RX DAY 160): SKIN BIOPSY: CHRONIC NON SPECIFIC DERMATITIS

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の女性（イスラエル）であり，重篤な有害事象の鼻中隔弯曲が認められた。関連する病歴は，左側潰瘍性大腸炎及び鼻中隔弯曲であった。被験者は非喫煙者及び非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，鼻中隔弯曲が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，鼻中隔弯曲は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は待機手術（ジアテルミーによる粘膜下層剥離術及び鼻甲介骨切除術）のために入院した。鼻中隔弯曲による鼻閉塞が認められた。被験者の症状は，吸入時の不快感であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Acamol（アセトアミノフェン）及び Optalgin が投与された。

The patient's past medications include:

SIMVASTATIN for HIGH CHOLESTEROL ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Deviated nasal septum (10012573) (Nasal septum deviation (10028762)) [v.20.1] [10012573]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of DEVIATED NASAL SEPTUM

- Investigator: Elective surgery

- AbbVie: Event more likely related to subject's prior medical history of deviated nasal septum (started 20[redacted]).

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の女性（イスラエル）であり，重篤な有害事象の角層下膿疱性皮膚症が認められた。関連する病歴は，炎症性腸疾患及び左側潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，角層下膿疱性皮膚症が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，発疹がみられ始めた。20[redacted] 年 [redacted] 月 [redacted] 日，発疹が悪化した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，胴体に乾癬状の発疹が認められた。治療として局所軟膏剤が塗布され，入院中に写真撮影が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，皮膚生検の結果，表在性及び深在性の化膿性毛包炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，さらに皮膚生検が実施され，慢性的な非特異的皮膚炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，S 状結腸鏡検査の結果，潰瘍性大腸炎が認められ，同日に被験者は退院した。

治療薬として Coal tar，ヒドロコルチゾン軟膏剤，Dermovate（クロベタゾールプロピオン酸エステル），及び Lyclear が投与された。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Subcorneal pustular dermatosis (10042342) (Subcorneal pustular dermatosis (10042342)) [v.20.1] [10042342]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: No

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of SUBCORNEAL PUSTULAR DERMATOSIS

- Investigator: N/A

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] SIGMOIDOSCOPY: Ulcerative colitis

[redacted] 20[redacted] SKIN BIOPSY: Superficial and deep purulent folliculitis

[redacted] 20[redacted] SKIN BIOPSY: Chronic non specific dermatitis

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
前立腺腫大	X			
急性心筋梗塞	X			
血尿	X			
心筋虚血	X	X		
胸骨炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	6[redacted]	MALE	White

Medical History	Onset Year
SURGERY: APENDECTOMY	20[redacted]
SURGERY: INGUINAL HERNIA CORRECTION	20[redacted]
OTHER: BENIGN PROSTATIC HYPERPLASIA	20[redacted]
OTHER: HEARTBURN	20[redacted]
OTHER: CARDIAC CATHETERIZATION	20[redacted]
OTHER: BALANCED HYPERLIPIDEMIA	20[redacted]
OTHER: INACTIVE ISCHEMIC HEART DISEASE	NOT REPORTED
OTHER: NEPHROLITHIASIS INACTIVE	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted] / 1	[redacted] / 43	43
ADALIMUMAB 40 MG EVERY OTHER WEEK	40 MG	EOW	[redacted] / 57	[redacted] / 176	120

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACETYLSALICYLIC ACID	300 mg (milligram(s))	BID	Y-M: 20[redacted]
LANSOPRAZOLE	30 mg (milligram(s))	QD	Y-M: 20[redacted]
DILTIAZEM	120 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted]
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]
CILAZAPRIL	5 mg (milligram(s))	BID	Y-M: 20[redacted]
TAMSULOSIN	0.4 mg (milligram(s))	QD	Y-M: 20[redacted]
ATORVASTATIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -172
BISACODYL	5 mg (milligram(s))	BID	Y-M: 20[redacted] / -44
SODIUM PICOSULFATE	2 SACHETS	Other: ONCE	Y-M: 20[redacted] / -43
FENTANYL	50 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / -42
MIDAZOLAM	2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -42
PROPOFOL	70 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / -42
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -35
RIFAMPICIN	300 mg (milligram(s))	BID	Y-M: 20[redacted] / -32
PREDNISONE	35 mg (milligram(s))	QD	Y-M: 20[redacted] / -28
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -21
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -17
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -12

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
ACETYLSALICYLIC ACID	300 mg (milligram(s))	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 112
LANSOPRAZOLE	30 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
DILTIAZEM	120 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 149
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
TAMSULOSIN	0.4 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 122
CILAZAPRIL	5 mg (milligram(s))	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 161
ATORVASTATIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
RIFAMPICIN	300 mg (milligram(s))	BID	Y-M: 20[redacted] / -32	Y-M: 20[redacted] / 61
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 44
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 50
FEXOFENADINE	160 mg (milligram(s))	QD	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 80
BETAMETHASONE	0.1 % (percent)	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 99
ACETYLSALICYLIC ACID	300 mg (milligram(s))	BID	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 149
METOCLOPRAMIDE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 150
TRAMADOL	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 150
BLOOD AND RELATED PRODUCTS	2 BLOOD TRANSFUSIONS	Other: ONCE	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 152
FESOTERODINE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / 150	Y-M: 20[redacted] / 150
BISOPROLOL	1.25 mg (milligram(s))	QD	Y-M: 20[redacted] / 153	ONGOING
ACETYLSALICYLIC ACID	300 mg (milligram(s))	QD	Y-M: 20[redacted] / 162	ONGOING
CILAZAPRIL	2.5 mg (milligram(s))	BID	Y-M: 20[redacted] / 162	ONGOING
DILTIAZEM	100 mg (milligram(s))	QD	Y-M: 20[redacted] / 162	ONGOING

ISOSORBIDE MONONITRATE	20 mg (milligram(s))	BID	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 164
BLOOD AND RELATED PRODUCTS	2 TRANSFUSION	Other: ONCE	Y-M: 20[redacted] / 186	Y-M: 20[redacted] / 187
CIPROFLOXACIN	500 mg (milligram(s))	Other: UNKNOWN	Y-M: 20[redacted] / 194	Y-M: 20[redacted] / 196
CEFAZOLIN	1 g (gram(s))	BID	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 197
BROTIZOLAM	0.25 mg (milligram(s))	QD	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 206
METAMIZOLE	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 207
METOCLOPRAMIDE	10 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 197	Y-M: 20[redacted] / 197
PORTALAK	30 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted] / 197	Y-M: 20[redacted] / 197
TRAMADOL	100 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 197	Y-M: 20[redacted] / 197
FEXOFENADINE	180 mg (milligram(s))	QD	Y-M: 20[redacted] / 197	Y-M: 20[redacted] / 200
FENTANYL	50 mcg (microgram(s))	QD	Y-M: 20[redacted] / 197	Y-M: 20[redacted] / 206
TRAMADOL	100 mg (milligram(s))	BID	Y-M: 20[redacted] / 198	Y-M: 20[redacted] / 202
VANCOMYCIN	1000-3000 mg (milligram(s))	Other: QD-BID	Y-M: 20[redacted] / 198	Y-M: 20[redacted] / 204
PORTALAK	30 mL (millilitre(s))	Other: ONCE	Y-M: 20[redacted] / 199	Y-M: 20[redacted] / 199
METAMIZOLE	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / 199	Y-M: 20[redacted] / 206
METAMIZOLE	2000 mg (milligram(s))	BID	Y-M: 20[redacted] / 204	ONGOING
RIFAMPICIN	600 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 205	Y-M: 20[redacted] / 205
SULFAMETHOXAZOLE	800 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 205	Y-M: 20[redacted] / 205
TRIMETHOPRIM	160 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 205	Y-M: 20[redacted] / 205
TRAMADOL	100 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 205	Y-M: 20[redacted] / 231

Event #1: Serious Adverse Event

Event Description	ENLARGED PROSTATE WORSENING
Preferred term	前立腺腫大
AE Onset Date / Rx Day	[redacted]20[redacted] / 73
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 122): PROSTATECTOMY: RESULVED WITH SEQUELA (DESCRIBED AS ANOTHER AE "HEMATORIA")	
AE Stopped Rx Day	124
Duration of AE	52 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	MEDICAL HISTORY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	ACUTE NON ST ELEVATION MYOCARDIAL INFRACTION
Preferred term	急性心筋梗塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 149
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	152
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the	NO

Event	
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #3: Serious Adverse Event

Event Description	HEMATURIA
Preferred term	血尿
AE Onset Date / Rx Day	[redacted]20[redacted] / 149
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	156
Duration of AE	8 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	PROSTATECTOMY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	CHRONIC ISCHEMIC HEART DESEASE - TRIPLE-VESSEL DISEASE
Preferred term	心筋虚血
AE Onset Date / Rx Day	[redacted]20[redacted] / 152
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	

[redacted]20[redacted] (RX DAY 179): LEFT HEART CARDIAC CATHETERIZATION: UNSUCCESSFUL; [redacted]20[redacted] (RX DAY 183): (AORTO)CORONARY BYPASS OF ONE CORONARY A: SUCCESSFUL; EXTRACORPOREAL CIRCULATION AUXILIARY TO: SUCCESSFUL; DOUBLE INTERNAL MAMMARY-CORONARY ARTERY: SUCCESSFUL; [redacted]20[redacted] (RX DAY 186): BLOOD TRANSFUSIONS: N/A; [redacted]20[redacted] (RX DAY 187): BLOOD TRANSFUSIONS: N/A

AE Stopped Rx Day	248 (72 DAYS AFTER LAST TREATMENT)
Duration of AE	97 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	INACTIVE ISCHEMIC HEART DISEASE IN MEDICAL HISTORY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Event #5: Serious Adverse Event

Event Description	INFECTION IN STERNUM
Preferred term	胸骨炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 194 (18 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	204 (28 DAYS AFTER LAST TREATMENT)
Duration of AE	11 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	CAGB SURGERY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（イスラエル）であり，重篤な有害事象の慢性虚血性心疾患（3 枝病変），非 ST 上昇型急性心筋梗塞，及び血尿が認められた。関連する病歴は，左側潰瘍性大腸炎，心臓カテーテル，高コレステロール血症，非活動性虚血性心疾患，良性前立腺肥大症，及び非活動性腎結石症であった。被験者は非喫煙者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，重篤な前立腺腫大の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，前立腺摘除術が実施された。

20[redacted] 年 [redacted] 月 [redacted] 日，非 ST 上昇型急性心筋梗塞及び血尿が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，慢性虚血性心疾患（3 枝病変）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，非 ST 上昇型急性心筋梗塞は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，血尿は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，慢性虚血性心疾患（3 枝病変）は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は血尿及び前立腺摘除術後の疼痛のため入院した。泌尿器洗浄が実施された。ヘモグロビン値は 14 から 9.4 に減少し，最終的には 11 に安定した。

入院中，胸痛，不快感，及び呼吸困難が認められた。検査の結果，被験者は非 ST 上昇型急性心筋梗塞と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，2 本のカテーテルを用いた冠動脈造影検査が実施された。処置は成功せず，被験者は心臓外科に転送された。冠動脈バイパス術が 3 回実施され，手術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

輸血が実施された（20[redacted] 年 [redacted] 月 [redacted] 日～20[redacted] 年 [redacted] 月 [redacted] 日，20[redacted] 年 [redacted] 月 [redacted] 日～20[redacted] 年 [redacted] 月 [redacted] 日）。

治療薬としてアスピリン，Cilaril，Mononit，Cartia（ジルチアゼム塩酸塩），フェソテロジンフマル酸塩，Pramin（メトクロプラミド），及びトラマドールが投与された。

Causality for HUMIRA (Blinded)

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1) Ischemic heart disease (10055218) (Myocardial ischaemia (10028600)) [v.22.0] [10055218]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Non ST segment elevation myocardial infarction (10064347) (Acute myocardial infarction (10000891)) [v.22.0] [10064347]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

3) Hematuria (10019450) (Haematuria (10018867)) [v.22.0] [10019450]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of CHRONIC ISCHEMIC HEART DESEASE - TRIPLE-VESSEL

- Investigator: Inactive ischemic heart disease in medical history.

- AbbVie: Risk factors include pre-existing ischemic heart disease and hyperlipidemia.

Event of ACUTE NON ST ELEVATION MYOCARDIAL INFRACTION

- Investigator: Unknown

- AbbVie: Risk factors include pre-existing ischemic heart disease and hyperlipidemia.

Event of HEMATURIA

- Investigator: Prostatectomy

- AbbVie: Risk factors include recent prostatectomy in [redacted] 20[redacted] and pre-existing history of nephrolithiasis,

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] electrocardiogram: Normal

Unknown date HBG: 14 No Units

Unknown date HBG: 9.4 No Units

Unknown date HBG: 11 No Units
Investigator No.:[redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（イスラエル）であり，重篤な有害事象の前立腺肥大の悪化が認められた。関連する病歴は，前立腺腫大及び良性前立腺肥大症であった。被験者は非喫煙者であった。
20[redacted] 年 [redacted] 月，前立腺肥大の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，前立腺肥大の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，前立腺摘除術が実施された。前立腺摘除術後の治癒及び経過観察のため，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日まで入院した。
治療薬として Promnix（タムスロシン塩酸塩）が投与された。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

RIFAMPICIN for LATENT TB ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Enlarged prostate (10049240) (Prostatomegaly (10051482)) [v.20.0] [10049240]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ENLARGED PROSTATE WORSENING

- Investigator: Medical history

- AbbVie: The patient has known medical history of BPH.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（イスラエル）であり，重篤な有害事象の胸骨感染が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，胸骨感染が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，胸骨感染は回復した。
冠動脈バイパス術後，胸骨部位に疼痛が認められた。3 日間の抗生剤（Ciproxin）経口投与による治療後，胸骨感染による創傷からの体液分泌が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，抗生剤（バンコマイシン）の静脈内投与が行われた。前立腺腫大の治療薬として，20[redacted] 年 [redacted] 月 [redacted] 日より被験者は Promnix（タムスロシン塩酸塩）0.4 mg を併用して毎日服用した。被験者の体調は良くなり，20[redacted] 年 [redacted] 月 [redacted] 日に被験者は退院した。
治療薬としてバンコマイシン，フェンタニル，トラマドール，Optalgin，スルファメトキサゾール，Cefamezine，Tramadex（トラマドール塩酸塩），Ciproxin，及び dipyrone が投与された。

The patient's past medications include:

MICROPIRIN (Aspirin) for INACTIVE ISCHEMIC HEART DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Pentasa for ULCERATIVE COLITIS (Started [redacted] 20[redacted])

Prednisone for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [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 HUMIRA (Open Label)

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1) Sternitis (10064110) (Sternitis (10064110)) [v.19.0] [10064110]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of INFECTION IN STERNUM

- Investigator: CAGB SURGERY

- AbbVie: RELATED TO CAGB SURGERY.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Rectum: 3 = Severe disease (spontaneous bleeding, ulceration)

Sigmoid: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Presence of friability: Yes

Subscore: 3

[redacted] 20[redacted] Flexible sigmoidoscopy:

Rectum: 3 = Severe disease (spontaneous bleeding, ulceration)

Sigmoid: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Presence of friability = Yes

Subscore: 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
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	4[redacted]	MALE	White

Medical History	Onset Year
MIGRAINE HEADACHE	20[redacted]
OTHER: H. PYLORI	20[redacted]
DRUG ALLERGIES/REACTIONS: PENICILIN ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 99	43

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MERCAPTOPURINE	100 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -96
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -76
AMOXICILLIN	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / -34
CLARITHROMYCIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / -34
ESOMEPRAZOLE	40 mg (milligram(s))	BID	Y-M: 20[redacted] / -34
TINIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / -34
STOMACAIN	1 BOTTLE	BID	Y-M: 20[redacted] / -14
FENTANYL	100 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / -13
MIDAZOLAM	5 mg (milligram(s))	Other: ONCE	Y-M: 20[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
PREDNISONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 56
FENTANYL	100 mcg (microgram(s))	Other: ONCE	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
MIDAZOLAM	7 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 81
GLAFENINE	250, 250, 65 mg (milligram(s))	PRN	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 86
PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 90
AMOXICILLIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 93
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 96
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 104
MIDAZOLAM	2 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 102	Y-M: 20[redacted] / 102
PROPOFOL	90 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted] / 102	Y-M: 20[redacted] / 102

METRONIDAZOLE	250 mg (milligram(s))	BID	Y-M: 20[redacted] / 102	Y-M: 20[redacted] / 105
HYDROCORTISONE	100 mg (milligram(s))	TID	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 109
PREDNISONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 109	ONGOING

Event #1: Serious Adverse Event

Event Description	UC WORSENING
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 61
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	109 (10 DAYS AFTER LAST TREATMENT)
Duration of AE	49 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UC WORSENING
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（イスラエル）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）及びヘリコバクター・ピロリ感染であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，直腸出血及び高頻度の排便（主に血液）の症状を含む潰瘍性大腸炎の悪化（再燃）により，最低 5 日間のコルチコステロイド投与を受けるため被験者は入院した。内視鏡検査が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Metrogyl（メトロニダゾール），ヒドロコルチゾン，及び prednisone が投与された。

The patient's past medications include:

PURINETHOL for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

RAFASSAL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

---

1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of UC WORSENING

- Investigator: UC Worsening.

- AbbVie: The event is exacerbation of underlying disease.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	5[redacted]	MALE	White

Medical History	Onset Year
CORONARY ARTERY DISEASE: CORONARY ARTERY DISEASE BIVASAL	20[redacted]
DIABETES MELLITUS	20[redacted]
HYPERLIPIDEMIA: HYPERCHOLESTEROLEMIA	20[redacted]
HYPERTENSION	20[redacted]
MYOCARDIAL INFARCTION	20[redacted]
SURGERY: CORONARY ANGIOPLASTY WITH STENT PLACEMENT OF 2 LEFT	20[redacted]
SURGERY: CORONARY ANGIOPLASTY WITH STENT PLACEMENT OF 3 RIGHT	20[redacted]
SURGERY: FISTULA OF THE SACRED	20[redacted]
INFLAMMATORY BOWEL DISEASE: HOSPITALIZATION FOR WORSENING OF RCU.	20[redacted]
LIVER DISEASE (EXCLUDING HEPATITIS): HEPATOMEGALY WITH STEATOSY	20[redacted]
OTHER: HYPOALBUMINEMIA	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	3	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 59	[redacted]20[redacted] / 88	30

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACETYLSALICYLIC ACID	100 mg (milligram(s))	QD	Y-M: 20[redacted]
LANSOPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted]
ZOFENOPRIL	15 mg (milligram(s))	QD	Y-M: 20[redacted]
CARVEDILOL	6.25 mg (milligram(s))	BID	Y-M: 20[redacted]
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted] / -142
ROSUVASTATIN	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -72
DOCUSATE	120 mg (milligram(s))	QD	Y-M: 20[redacted] / -46
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -45
ISONIAZID	300 mg (milligram(s))	QD	Y-M: 20[redacted] / -34
METFORMIN	2550 mg (milligram(s))	QD	Y-M: 20[redacted] / -3

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ACETYLSALICYLIC ACID	100 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
LANSOPRAZOLE	20 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
ZOFENOPRIL	15 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
CARVEDILOL	6.25 mg (milligram(s))	BID	Y-M: 20[redacted]	ONGOING
MESALAZINE	1200 mg (milligram(s))	TID	Y-M: 20[redacted] / -142	ONGOING
ROSUVASTATIN	20 mg (milligram(s))	QD	Y-M: 20[redacted] / -72	ONGOING
ISONIAZID	300 mg (milligram(s))	QD	Y-M: 20[redacted] / -34	Y-M: 20[redacted] / 252
METFORMIN	2550 mg (milligram(s))	QD	Y-M: 20[redacted] / -3	ONGOING

PREDNISONE	12.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 71
INSULIN GLARGINE	6 IU (international unit(s))	QD	Y-M: 20[redacted] / 60	ONGOING
PREDNISONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 86
PREDNISONE	7.5 mg (milligram(s))	QD	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 98
PARACETAMOL	1000 mg (milligram(s))	QD	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 93
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted] / 99	ONGOING

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

Event Description	WORSENING OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 91 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 101): TERMINAL ILEOSTOMY: COMPLETE; TOTAL COLECTOMY: PROCEDURE COMPLETED WITH NOT ADDITIONAL PROCEDURE	
AE Stopped Rx Day	109 (21 DAYS AFTER LAST TREATMENT)
Duration of AE	19 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	LACK OF EFFICACY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（イタリア）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）及び脂肪症を伴う肝腫大であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，排便頻度の増加，発熱，腹痛，及び直腸出血が認められ，被験者は入院した。入院歴聴取及び身体所見では，虚血性心疾患及び糖尿病患者にみられる再発 RCU が示唆された。20[redacted] 年 [redacted] 月 [redacted] 日，結腸全摘術が実施され，終末型回腸瘻が造設された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Tachipirina（アセトアミノフェン）が投与された。

Causality for HUMIRA (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.22.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: LACK OF EFFICACY

- AbbVie: The event is exacerbation of underlying disease of UC

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
関節痛	X			
肺気腫	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	5[redacted]	MALE	White

Medical History	Onset Year
OTHER: IDIOPATHIC URTICARIA	20[redacted]
ANEMIA: LOW HEMOGLOBIN LOW SERUM IRON	20[redacted]
OTHER: PLEURAL EFFUSION	20[redacted]
HYPERTENSION: PREDOMINANTLY DIASTOLIC ARTERIAL HYPERTENSION	20[redacted]
LIVER DISEASE (EXCLUDING HEPATITIS): STEATOSI	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	39	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

ADALIMUMAB 40 MG 40 MG EVERY WEEK	EW	[redacted]20[redacted] / 60 [redacted]20[redacted] / 379	320

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CETIRIZINE	10 mg (milligram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted] / -308
FOLIC ACID	15 mg (milligram(s))	QD	Y-M: 20[redacted] / -43
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / -43
DOCUSATE	120 mL (millilitre(s))	QD	Y-M: 20[redacted] / -14
FOLIC ACID	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -13
IRON	14 mg (milligram(s))	QD	Y-M: 20[redacted] / -12

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
CETIRIZINE	10 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
PANADEINE CO	500 mg (milligram(s))	Other: ON DEMAND	Y-M: 20[redacted] / 342	Y-M: 20[redacted] / 342
BETAMETHASONE	0.5 mg (milligram(s))	BID	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 344
CETIRIZINE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 344
RANITIDINE	300 mg (milligram(s))	QD	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 344
DOCUSATE	120 mL (millilitre(s))	QD	Y-M: 20[redacted] / 345	Y-M: 20[redacted] / 345
ASCORBIC ACID W/FERRIC PYROPHOSPHATE	1 CP UNKNOWN	QD	Y-M: 20[redacted] / 347	ONGOING
COLECALCIFEROL	2.5 mL (millilitre(s))	Other: 1 VIAL EVERY WEEK	Y-M: 20[redacted] / 347	ONGOING
FOLIC ACID	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 347	ONGOING
MESALAZINE	800 mg (milligram(s))	TID	Y-M: 20[redacted] / 347	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	TID	Y-M: 20[redacted] / 382	ONGOING

Event #1: Serious Adverse Event

Event Description	POLYARTHRALGIAS
Preferred term	関節痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 335
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	BULLOUS PULMONARY EMPHYSEMA
Preferred term	肺気腫
AE Onset Date / Rx Day	[redacted]20[redacted] / 335
Age at AE Onset	5[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 344): HEMATOCRIT: 0.41 [0.42 - 0.52] FRACTION; HEMOGLOBIN: 129 [140 - 180] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 2.31 [NOT REPORTED - 0.3] MG/DL; RHEUMATOID FACTOR: 10.0 [NOT REPORTED - 20] IU/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 345): COMPUTERIZED AXIAL TOMOGRAPHY CHEST: BULLOUS PULMONARY EMPHYSEMA

AE Stopped Rx Day	365
Duration of AE	31 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED

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

Generated: [redacted] 20[redacted]:02:12
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（イタリア）であり，重篤な有害事象の嚢胞性肺気腫及び多発性関節痛が認められた。関連する病歴は，胸水及び拡張期優位の動脈性高血圧であった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 39 年）であった。
20[redacted] 年[redacted] 月[redacted] 日，非重篤な無力症が認められた（継続中）。
20[redacted] 年[redacted] 月[redacted] 日，嚢胞性肺気腫及び多発性関節痛が認められた。20[redacted] 年[redacted] 月[redacted] 日，嚢胞性肺気腫は回復した。
20[redacted] 年[redacted] 月[redacted] 日，被験者は入院し，多発性関節痛が認められた（潰瘍性大腸炎の既往歴を有していた）。症状には，呼吸困難，軽度の発熱，及び胸痛が含まれた。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。
治療薬として Tachidol が投与された。

The patient's past medications include:

AZATIOPRINA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DELTACORTENE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [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 HUMIRA 40MG/0.8ML (Blinded)

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1) Emphysematous bulla (10050776) (Emphysema (10014561)) [v.22.0] [10050776]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Yes

2) Polyarthralgia (10036029) (Arthralgia (10003239)) [v.22.0] [10036029]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of BULLOUS PULMONARY EMPHYSEMA

- Investigator: N/A

- AbbVie: N/A

Event of POLYARTHRALGIAS

- Investigator: N/A

- AbbVie: The patient has known history of smoking and hypertension.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CAT chest:

- Shaded glass frosted with thickening base left and spill pleural. Spontaneous resolution of symptoms.

[redacted] 20[redacted] Computerized axial tomography chest: bullous pulmonary emphysema

[redacted] 20[redacted] high sensitivity c reactive protein: 2.31 mg/dL (normal <0.30)

[redacted] 20[redacted] rheumatoid factor: 10.0 IU/ml (normal <20.00)

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	4[redacted]	MALE	White

Medical History	Onset Year
CHOLELITHIASIS	20[redacted]
OTHER: PARAPSORIATIC SKIN MANIFESTATIONS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	UNKNOWN			
CIGARETTES	FORMER	0.5 PACKS	23	20[redacted]
CIGARS	UNKNOWN			
PIPES	UNKNOWN			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44
ADALIMUMAB TDM	40 MG	EOW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56	1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	10 mg/kg (milligram(s)/kilogram)	Other: EVERY 8 WEEK	Y-M: 20[redacted]
SULFASALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -190
BECLOMETASONE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / -160
MOVIPREP	110 g (gram(s))	QD	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SULFASALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -190	ONGOING
MESALAZINE	500 mg (milligram(s))	QD	Y-M: 20[redacted] / 61	ONGOING
PARACETAMOL	1 g (gram(s))	QD	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 62
METHYLPREDNISOLONE	60 mg (milligram(s))	QD	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 66

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

Event Description	UC WORSENING
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 60 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 61): HEMATOCRIT: 0.38 [0.39 - 0.52] FRACTION; HEMOGLOBIN: 133 [135 - 172] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 5 [0 - 10] MG/L; [redacted]20[redacted](RX DAY 65): HEMATOCRIT: 0.39 [0.39 - 0.52] FRACTION; HEMOGLOBIN: 133 [135 - 172] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 1.5 [0 - 10] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 61): ABDOMINAL CT: THICKNESS INCREASE OF SIGMA AND RECTUM WALL

AE Stopped Rx Day	65 (9 DAYS AFTER LAST TREATMENT)
Duration of AE	6 DAYS
Severity	Moderate

Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ULCERATIVE COLITIS FLARE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（イタリア）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日の夕方遅くより，嘔吐を伴う強い腹痛（左下腹部）がみられ始めた。ひどい疼痛のため，被験者は救急治療室を受診した。被験者は救急治療室に数時間滞在した後，午前 4 時頃に消化器内科病棟へ入院した。（20[redacted] 年 [redacted] 月 [redacted] 日）。腹痛及び嘔吐に伴う兆候及び症状が認められた。鎮痛療法が施された後に疼痛は軽減し，嘔吐及び他の症状はみられなかった。入院中にステロイド剤の全身投与が開始され，腹痛は軽減した。本報告時には軽度の腹痛が認められた。近日中に結腸切除術が実施される予定であった。

治療薬として Asacol（メサラジン），Urbason，Medrol（メチルプレドニゾロン），Pentacol（メサラジン），及び Perfalgan（アセトアミノフェン）が投与された。

The patient's past medications include:

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BECLOMETHASONE DIPROPIONATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of UC WORSENING

- Investigator: Ulcerative colitis flare

- AbbVie: This event is exacerbation of underlying disease of UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Abdominal CT: Thickness increase of sigma and rectum wall

[redacted] 20[redacted] CRP: 0.50 mg/dL (normal 0.0 to < 1.0)

[redacted] 20[redacted] Hematocrit: 38.2 % (normal 39.0 to 52.0)

[redacted] 20[redacted] Hematocrit: 38.5 % (normal 39.0 to 52.0)

[redacted] 20[redacted] HGB: 13.3 g/dL (normal 13.5 to 17.2)

[redacted] 20[redacted] HGB: 13.3 (normal 13.5 to 17.2)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
好中球数減少		X		
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	2[redacted]	FEMALE	Asian

Medical History	Onset Year
OTHER: ALLERGY TO STRAWBERRIES	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 36	36
ADALIMUMAB 4040 MG MG EVERY OTHER WEEK		EOW	[redacted]20[redacted] / 55	[redacted]20[redacted] / 147	93

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	800 mg (milligram(s))	TID	Y-M: 20[redacted]
ESCHERICHIA COLI	320 mg (milligram(s))	BID	Y-M: 20[redacted] / -290
PREDNISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / -276
BECLOMETASONE	3 mg (milligram(s))	QD	Y-M: 20[redacted] / -128
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -128
METHYLPREDNISOLONE	60 mg (milligram(s))	QD	Y-M: 20[redacted] / -107
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / -107
INFLIXIMAB	5 mg/kg (milligram(s)/kilogram)	Other: EVERY 8 WEEKS	Y-M: 20[redacted] / -79
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	Y-M: 20[redacted] / -66
METHYLPREDNISOLONE	4 mg (milligram(s))	QD	Y-M: 20[redacted] / -23
MOVIPREP	110 g (gram(s))	QD	Y-M: 20[redacted] / -9
MIDAZOLAM	3 mg (milligram(s))	QD	Y-M: 20[redacted] / -8
PETHIDINE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ELECTROLYTE SOLUTIONS	500 mL (millilitre(s))	QD	Y-M: 20[redacted] / 215	Y-M: 20[redacted] / 216
METRONIDAZOLE	200 mg (milligram(s))	BID	Y-M: 20[redacted] / 219	Y-M: 20[redacted] / 229
GENTAMICIN	UNK g (gram(s))	QD	Y-M: 20[redacted] / 222	Y-M: 20[redacted] / 238
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 238
SULFASALAZINE	1 g (gram(s))	BID	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 234

SULFASALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted]- [redacted] / 235	ONGOING

Event #1: AE Leading to Discontinuation of Study Drug

Event Description	DECREASE IN ABSOLUTE NEUTROPHIL BLOOD COUNT EXAMINATION
Preferred term	好中球数減少
AE Onset Date / Rx Day	[redacted]20[redacted] / 148 (1 DAY 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	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	UC WORSENING
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 215 (68 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 215): HEMOGLOBIN: 110 [120 - 175] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 10.6 [0 - 10] MG/L; RED BLOOD COUNT: 4 [4 - 5.6] X10^12/L; WHITE BLOOD COUNT: 6.8 [4 - 10] X10^9/L; [redacted]20[redacted] (RX DAY 220): HIGH-SENSITIVITY C-REACTIVE PROTEIN: 16.5 [0 - 10] MG/L; SIDEREMIA: 23 [50 - 170] MCG/DL; [redacted]20[redacted] (RX DAY 231): SIDEREMIA: 34 [50 - 170] MCG/DL; [redacted]20[redacted] (RX DAY 238): HEMOGLOBIN: 111 [120 - 158] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 2.6 [0 - 10] MG/L; RED BLOOD COUNT: 3.9 [4 - 5.2] X10^12/L; WHITE BLOOD COUNT: 4.8 [4 - 10] X10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 223): Stool CLOSTRIDIUM DIFFICILE SEARCH: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 215): ABDOMEN CT SCAN: SLIGHTLY SHADED THICKENING OF THE SIGMOID WALLS;

PRESENCE OF LYMPH NODE SIZE INCREASED IN THE LUMBAR-AORTIC, INTER-AORTO-CAVAL AND GROIN; [redacted]20[redacted](RX DAY 224): CHEST X-RAY: NO CLOUDING PARENCHYMAL INFLAMMATION. NO PLEURAL EFFUSIONS. CARDIO-MEDIASTINAL WITHIN IMAGE; [redacted]20[redacted] (RX DAY 229): COLONOSCOPY: THE LEFT COLON FROM THE RECTUM HAS SEVERELY INFLAMED MUCOSA WITH EROSIONS / SUPERFICIAL ULCERATIONS AND FIBRIN AND PRESENCE OF PURULENT PUS. BOWELS TUBULIZZATO, SLIGHTLY DISTENSIBLE. BEYOND THE FLEXUR

AE Stopped Rx Day	238 (91 DAYS AFTER LAST TREATMENT)
Duration of AE	24 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	ULCERATIVE COLITIS FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（イタリア）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］／全大腸炎型）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は試験を中止した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められ，症状は排便頻度の増加，直腸出血，及び発熱であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。臨床検査及び診断検査が実施され，併用薬投与による治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Pantorc，電解質液，Deflamon（メトロニダゾール），Salazopyrin（サラゾスルファピリジン），及びゲンタマイシンが投与された。

The patient's past medications include:

PENTACOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ESCHERICHIA COLI NISSLE for ULCERATIVE COLITIS ([redacted])

DELTACORTENE for ULCERATIVE COLITIS ([redacted])

TOPSTER for ULCERATIVE COLITIS ([redacted])

METHYLPREDNISOLONE for ULCERATIVA COLITIS ([redacted])

PANTORC for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of UC WORSENING

- Investigator: Ulcerative colitis flare

- AbbVie: Worsening of underlying disease-ulcerative colitis

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMEN CT SCAN: Slightly shaded thickening of the sigmoid walls; presence of lymph node size increased in the lumbar-aortic, inter-aorto-caval and groin.

[redacted] 20[redacted] CHEST X-RAY: No clouding parenchymal inflammation. No pleural effusions. Cardio-mediastinal within image.

[redacted] 20[redacted] CLOSTRIDIUM DIFFICILE SEARCH: Negative

[redacted] 20[redacted] COLONOSCOPY: Rectum 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions) Sigmoid 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions) Descending colon 1 = Mild disease (erythema, decreased vascular pattern, mild friability) Transverse colon 1 = Mild disease (erythema, decreased vascular pattern, mild friability) Ascending colon/cecum 1 = Mild disease (erythema, decreased vascular pattern, mild friability) Presence of friability? Yes Subscore 2

[redacted] 20[redacted] COLONOSCOPY: The left colon from the rectum has severely inflamed mucosa with erosions / superficial ulcerations and fibrin and presence of purulent pus. Bowels tubulizzato, slightly distensible. Beyond the flexure left bowels normal.

[redacted] 20[redacted] ELECTROCARDIOGRAM: Normal

[redacted] 20[redacted] ENDOSCOPY: Type of procedure Flexible sigmoidoscopy Rectum 0 = Normal or inactive disease Sigmoid 0 = Normal or inactive disease Descending colon 0 = Normal or inactive disease Transverse colon Ascending colon/cecum Presence of friability? No Subscore 0

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 1.65 mg/dL (normal 0 to 1.0)

[redacted] 20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.26 mg/dL (normal 0 to 1.0)

[redacted] 20[redacted] RBC (HEMATOLOGY): 3.97 X10**6/MCL (normal 4.0 to 5.6)

[redacted] 20[redacted] RBC (HEMATOLOGY): 3.93 X10**6/MCL (normal 4.0 to 5.6)

[redacted] 20[redacted] SIDEREMIA: 23 mg/dL (normal 50 to 170)

[redacted] 20[redacted] SIDEREMIA: 34 mg/dL (normal 50 to 170)

[redacted] 20[redacted] WBC (HEMATOLOGY): 6.75 X10**3/MCL (normal 4 to 10)

[redacted] 20[redacted] WBC (HEMATOLOGY): 4.81 X10**3/MCL (normal 4 to 10)

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
非小細胞肺癌	X	X	X	

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	6[redacted]	MALE	White

Medical History	Onset Year
DIABETES MELLITUS: INSULINE DEPENDANT	19[redacted]
SURGERY: BACK BONE FRACTURE	20[redacted]
OTHER: HYPERCHOLESTROLEMIA	20[redacted]
HYPERTENSION	20[redacted]
MYOCARDIAL INFARCTION: WITH ANGIOPLASTY AND STENTING	20[redacted]
OTHER: RENAL DISFUNCTION	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2.5 PACKS	44	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2-4 drinks per day

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

ADALIMUMAB 4040 MG MG EVERY OTHER WEEK	EOW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 141	84

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SIMVASTATIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]
GLIMEPIRIDE	4 mg (milligram(s))	QD	Y-M: 20[redacted]
METFORMIN	1000 mg (milligram(s))	BID	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	80 mg (milligram(s))	QD	Y-M: 20[redacted]
BISOPROLOL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]
ENALAPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted]
FUROSEMIDE	20 mg (milligram(s))	QD	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
CHLORTALIDONE	12.5 mg (milligram(s))	QD	Y-M: 20[redacted]
INSULIN ASPART	DOSE DEPENDENT ON GLUCOSE LEVELS IU (international unit(s))	PRN	Y-M: 20[redacted]
INSULIN GLARGINE	DOSE DEPENDENT ON GLUCOSE LEVELS IU (international unit(s))	PRN	Y-M: 20[redacted]
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted] / -189
LOPERAMIDE	8 mg (milligram(s))	PRN	Y-M: 20[redacted] / -25

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
SIMVASTATIN	40 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
GLIMEPIRIDE	4 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
METFORMIN	1000 mg (milligram(s))	BID	Y-M: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	80 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
BISOPROLOL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
ENALAPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
FUROSEMIDE	20 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING

PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted]	ONGOING
CHLORTALIDONE	12.5 mg (milligram(s))	QD	Y-M: 20[redacted]- [redacted]	ONGOING
INSULIN ASPART	DOSE DEPENDENT ON GLUCOSE LEVELS IU (international unit(s))	PRN	Y-M: 20[redacted]- [redacted]	ONGOING
INSULIN GLARGINE	DOSE DEPENDENT ON GLUCOSE LEVELS IU (international unit(s))	PRN	Y-M: 20[redacted]- [redacted]	ONGOING
MESALAZINE	2 g (gram(s))	QD	Y-M: 20[redacted]- [redacted] / -189	Y-M: 20[redacted]-[redacted] / 218
LOPERAMIDE	8 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / -25	ONGOING
PARACETAMOL	500 mg (milligram(s))	PRN	Y-M: 20[redacted]- [redacted] / 66	ONGOING
CARBOPLATIN W/ETOPOSIDE	UNKNOWN UNITS UNKNOWN	Other: UNKNOWN FREQUENCY	Y-M: 20[redacted]- [redacted] / 162	ONGOING

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

Event Description	DISSEMINATED NON-SMALL CELL CARCINOMA PROBABLE PRIMARY LOCALISATION LUNG
Preferred term	非小細胞肺癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 144 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 156): ALANINE AMINO TRANSFERASE (SGPT/ALT): 14 [0 - 45] U/L; ALBUMIN: 37 [35 - 53] G/L; ALKALINE PHOSPHATASE: 129 [0 - 120] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 29 [0 - 35] U/L; CALCIUM: 2.47 [2.1 - 2.55] MMOL/L; CREATININE: 124 [59 - 104] MCMOL/L; EGFR: 54 [60 - NOT REPORTED] ML/MIN; GAMMA-GT: 25 [10 - 55] U/L; HEMATOCRIT: 0.37 [0.4 - 0.5] FRACTION; HEMOGLOBIN: 118 [137 - 177] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 77 [0 - 8] MG/L; LDH: 764 [0 - 248] U/L; LEUCOCYTES: 14.7 [4 - 10] X10^9/L; PLATELET COUNT: 525 [150 - 400] X10^9/L; POTASSIUM: 4.5 [3.4 - 4.5] MMOL/L; SEGM. ABSOLUTE: 11.2 [1.8 - 7.2] X10^9/L; SODIUM: 136 [136 - 145] MMOL/L; TOTAL BILIRUBIN: 4 [3 - 17] MCMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	227 (86 DAYS AFTER LAST TREATMENT)
Duration of AE	84 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	SMOKING

Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING, DEATH OF SUBJECT

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（オランダ）であり，重篤な有害事象で致死性の肺原発性とみられる播種性非小細胞癌が認められた。関連する病歴は，インスリン依存型糖尿病，高コレステロール血症，高血圧，及び左側潰瘍性大腸炎であった。被験者は元喫煙者（1 日当たり 2.5 箱，喫煙期間 44 年）であり，中等度のアルコール摂取者（1 日当たり 2～4 ドリンク）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，肺原発性とみられる播種性非小細胞癌が認められた。被験者は呼吸困難及び疲労による転倒後，長引く股関節痛のため病院を受診した。転倒後の長引く疼痛のため，X 線検査が実施された。腸骨稜の病変（おそらく転移性）が認められたため，その後被験者は整形外科医により内科専門医へ転送された。ポジトロン断層撮影／コンピュータ断層撮影検査の結果，左肺上葉，縦隔リンパ節，鎖骨上リンパ節，頸部リンパ節，胸骨，骨盤，及び寛骨臼に病変が認められた。顎下リンパ節の生検の結果，神経内分泌細胞の分化を伴った非小細胞癌が認められた。TTF-1 抗体免疫組織染色の陽性結果に基づき，原発部位はおそらく肺であると判断された。カルボプラチン／エトポシドによる緩和的化学療法が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死亡原因は播種性非小細胞癌として報告された。検死解剖実施の有無は不明である。

治療薬としてカルボプラチン／エトポシドが投与された。

Causality for HUMIRA (Open Label)

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1) Non-small cell lung cancer (10061873) (Non-small cell lung cancer (10061873)) [v.18.0] [10061873]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of DISSEMINATED NON-SMALL CELL CARINOMA PROBABLE PRIMARY LOCALISATION LUNG

- Investigator: Smoking

- AbbVie: Chronic smoking of 2.5 packs of cigarettes per day over 44 years in a 68 year old male.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] flexible sigmoidoscopy:

Rectum: severe disease(spontaneous bleeding, ulceration)

[redacted] 20[redacted] Flexible sigmoidoscopy:

Rectum: Severe disease (spontaneous bleeding, ulceration), Sigmoid: Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

[redacted] 20[redacted] High-sensitivity C-reactive protein: 77 MG/L (normal 0 to 8)

[redacted] 20[redacted] LDH: 764 U/L (normal 0 to 248)

[redacted] 20[redacted] Leucocytes: 14.7 X10**9/L (normal 4 to 10)

[redacted] 20[redacted] Platelet count: 525 X10**9/L (normal 150 to 400)

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
骨盤内炎症性疾患	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: IRRITABLE BOWEL SYNDROME	20[redacted]
OTHER: EASY BRUISING	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACKS	8	
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 36	36
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 52	[redacted]20[redacted] / 362	311

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FISH OIL	1 CAPSULE	QD	Y-M: 20[redacted]
TRYPTOPHAN, L-	1 CAPSULE	QD	Y-M: 20[redacted]
VITAMINS NOS	1 TABLET	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted] / -259
SPIRULINA SPP.	1 CAPSULE	QD	Y-M: 20[redacted] / -209
NUTRIENTS NOS	125 mL (millilitre(s))	BID	Y-M: 20[redacted] / -8
BISACODYL	5 mg (milligram(s))	BID	Y-M: 20[redacted] / -7
MOVIPREP	2 L (litre(s))	QD	Y-M: 20[redacted] / -6
FENTANYL	125 mcg (microgram(s))	QD	Y-M: 20[redacted] / -5
MIDAZOLAM	5 mg (milligram(s))	QD	Y-M: 20[redacted] / -5
ACETYLCYSTEINE	UNKNOWN UNKNOWN	Other: UNKNOWN	Y-M: 20[redacted] / -2
PARACETAMOL	1000 mg (milligram(s))	QID	Y-M: 20[redacted] / -2

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4.8 g (gram(s))	QD	Y-M: 20[redacted] / -259	ONGOING
PARACETAMOL	1000 mg (milligram(s))	BID	Y-M: 20[redacted] / 4	ONGOING
IBUPROFEN	NOT REPORTED	PRN	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 79
METRONIDAZOLE	NOT REPORTED	QD	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 79
OFLOXACIN	NOT REPORTED	QD	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 79
PARACETAMOL	1000 mg (milligram(s))	QID	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 83
MEROKEN NEW	2 SACHETS	BID	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 125
TRAMADOL	50 mg (milligram(s))	TID	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 125
CLINDAMYCIN	450 mg (milligram(s))	QID	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 93

Event #1: Serious Adverse Event

Event Description	PELVIC INFLAMMATORY DISEASE
Preferred term	骨盤内炎症性疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 72
Age at AE Onset	2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	83
Duration of AE	12 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（オランダ）であり，重篤な有害事象の骨盤内炎症性疾患が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，骨盤内炎症性疾患が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，骨盤内炎症性疾患は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，排尿障害，排便痛，及び骨盤痛の兆候及び症状がみられ，被験者は入院した。被験者は避妊手段なしの性交のリスク因子を有していた。被験者は淋菌感染による骨盤内炎症性疾患と診断され，抗生剤及び鎮痛剤の静脈内投与による治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，抗生剤の経口投与が継続された。

治療薬としてメトロニダゾール，トラマドール，イブプロフェン，及びオフロキサシンが投与された。

Causality for HUMIRA (Open Label)

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1) Pelvic inflammatory disease (10034254) (Pelvic inflammatory disease (10034254)) [v.18.1] [10034254]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of PELVIC INFLAMMATORY DISEASE

- Investigator: Unknown

- AbbVie: The cause of the event was reported

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
慢性炎症性脱髄性多発根ニューロパチー	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	5[redacted]	FEMALE	White

Medical History	Onset Year
SURGERY: HYSTERECTOMY	20[redacted]
ARTHRITIS: RHEUMATOID ARTHRITIS	20[redacted]
HYPERTENSION: 20[redacted]	20[redacted]
OSTEOARTHRITIS: [redacted]-[redacted]-20[redacted]	20[redacted]
OTHER: ADRENAL INSUFFICIENCY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.05 PACKS	44	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42

ADALIMUMAB TDM	40/40/40 MG	EOW/EOW/EW	[redacted]20[redacted] / 55	[redacted]20[redacted] / 239	185

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LEKOVIT CA	1 TABLET	QD	Y-M: 20[redacted]
MEBEVERINE	200 mg (milligram(s))	PRN	Y-M: 20[redacted]
MESALAZINE	4.5 g (gram(s))	QD	Y-M: 20[redacted]
PREDNISONE	50 mg (milligram(s))	QD	Y-M: 20[redacted]
PREDNISONE	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -251
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -105
FOSINOPRIL	10 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -14
HYDROCHLOROTHIAZIDE	UNKNOWN mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -14
BISACODYL	5 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / -10
MOVIPREP	1 L (litre(s))	QD	Y-M: 20[redacted]-[redacted] / -9
FENTANYL	100 mcg (microgram(s))	QD	Y-M: 20[redacted]-[redacted] / -8
MIDAZOLAM	5 mg (milligram(s))	QD	Y-M: 20[redacted]-[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
LEKOVIT CA	1 TABLET	QD	Y-M: 20[redacted]	ONGOING
MEBEVERINE	200 mg (milligram(s))	PRN	Y-M: 20[redacted]	ONGOING
FOSINOPRIL	20 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / 39	ONGOING
PREDNISONE	ONE DAY 5, OTHER DAY 2.5 mg (milligram(s))	Other: 5 AND 2.5 MG SWITCHING EVERY DAY, EVERY OTHER DAY	Y-M: 20[redacted]-[redacted] / 98	ONGOING
DESLORATADINE	5 mg (milligram(s))	PRN	Y-M: 20[redacted]-[redacted] / 154	Y-M: 20[redacted]-[redacted] / 198
NITROFURANTOIN	100 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 190	Y-M: 20[redacted]-[redacted] / 195
IMMUNOGLOBULIN HUMAN NORMAL	30 g (gram(s))	Other: INTRAVENOUS COURSE IN 3 DAYS	Y-M: 20[redacted]-[redacted] / 327	ONGOING

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

Event Description	CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY
Preferred term	慢性炎症性脱髄性多発根ニューロパチー
AE Onset Date / Rx Day	[redacted]20[redacted] / 188
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 188): EMG: RESULTS EMG: PROGRESSIVE POLYNEUROPATHY; [redacted]20[redacted] (RX DAY 252): EMG: POLYNEUROPATHY; [redacted]20[redacted] (RX DAY 272): EMG: POLYNEUROPATHY	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の女性（オランダ）であり，重篤な有害事象の慢性炎症性脱髄性多発神経炎（以下「CIDP」）が認められた。関連する病歴は，左側潰瘍性大腸炎，高血圧，関節リウマチ，及び副腎機能不全であった。被験者は元喫煙者（1 日当たり 0.05 箱，喫煙期間 44 年）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，CIDP が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者から 8 週間前に両手指先，全つま先，及び両足にピリピリ感がみられたとの報告があった。ピリピリ感は手及び前腕にも広がった。被験者によると，クッションの上を歩いている感覚があり，物を掴むことが困難であった。腕は重く感じられ，腕力は弱ま

っていた。その後，症状は進み，手を用いる細かな日常生活動作を行うことが困難となり，歩行困難となった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は神経科を受診し，多発神経炎と診断され，筋電図検査により CIDP と確定された。神経科医及び治験分担医師より，治験薬との因果関係が存在する可能性があるため，アダリムマブの投与中止が勧告された。

神経科医の診察及び筋電図検査の結果より，正式な診断として CIDP が確定された。20[redacted] 年 [redacted] 月 [redacted] 日，免疫グロブリンの静脈内投与による治療が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，CIDP が寛解したため治療は中止された。

治療薬として Nanogam（免疫グロブリン製剤）が投与された。

The patient's past medications include:

PREDNISON for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

SALOFALK for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

CORTIMENT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Chronic inflammatory demyelinating polyneuropathy (10077384) (Chronic inflammatory demyelinating polyradiculoneuropathy (10057645)) [v.22.0] [10077384]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: No

Alternative Etiology for HUMIRA (Blinded)

Event of CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

- Investigator: Not applicable.

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ELECTROCARDIOGRAM: Left axis deviation

[redacted] 20[redacted] EMG: progressive polyneuropathy.

[redacted] 20[redacted] EMG: POLYNEUROPATHY

[redacted] 20[redacted] EMG: POLYNEUROPATHY

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
悪性黒色腫	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	5[redacted]	MALE	White

Medical History	Onset Year
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: HYPERCHOLESTROLEMIA	20[redacted]
OTHER: CATARACT	20[redacted]
OTHER: CRAMPING LOWER LEGS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	31	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 359	304

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACETYLSALICYLIC ACID	80 mg (milligram(s))	QD	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -178
CALCIUM	330 mg (milligram(s))	BID	Y-M: 20[redacted] / -20
COLECALCIFEROL	5 mcg (microgram(s))	QD	Y-M: 20[redacted] / -20
MONASCUS PURPUREUS	1500 mg (milligram(s))	QD	Y-M: 20[redacted] / -20
MOVIPREP	1 L (litre(s))	QD	Y-M: 20[redacted] / -6
PROPOFOL	500 mg (milligram(s))	QD	Y-M: 20[redacted] / -5

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
ACETYLSALICYLIC ACID	80 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	3 g (gram(s))	QD	Y-M: 20[redacted]	ONGOING
CALCIUM	330 mg (milligram(s))	BID	Y-M: 20[redacted] / -20	ONGOING
COLECALCIFEROL	5 mcg (microgram(s))	QD	Y-M: 20[redacted] / -20	ONGOING
MONASCUS PURPUREUS	1500 mg (milligram(s))	QD	Y-M: 20[redacted] / -20	ONGOING
MINERALS NOS	3 DROPS	BID	Y-M: 20[redacted] / 72	ONGOING

Event #1: Serious Adverse Event

Event Description	MELANOMA
Preferred term	悪性黒色腫
AE Onset Date / Rx Day	[redacted]20[redacted] / 372 (13 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 393): EXCISION FACIAL SKIN MELANOMA: SUCCESFUL REMOVAL

AE Stopped Rx Day	393 (34 DAYS AFTER LAST TREATMENT)

Duration of AE	22 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	THE SUN/OUTSIDE WORK.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（オランダ）であり，重篤な有害事象の悪性黒色腫が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，悪性黒色腫が認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，疑わしい皮膚病変が認められ，悪性黒色腫の手術が実施された。組織検査の結果，悪性黒色腫であった。

The patient's past medications include:

BUDESONIDE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Melanoma (10053571) (Malignant melanoma (10025650)) [v.21.1] [10053571]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of MELANOMA

- Investigator: The sun/outside work.

- AbbVie: Not applicable.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	6[redacted]	FEMALE	White

Medical History	Onset Year
HYPERTENSION	20[redacted]
OTHER: POST MENOPAUSAL STATUS	20[redacted]
SURGERY: THYROIDECTOMY DUE TO GOITRE	20[redacted]
CHOLELITHIASIS: CHOLECYSTECTOMY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]0[redacted] / 47	47
ADALIMUMAB TDM	40/40/160/40/40 MG	EOW/EW/EW/EW/EW	[redacted]20[redacted] / 55	[redacted]20[redacted] / 294	240

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BISOPROLOL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]
LEVOTHYROXINE	100 mcg (microgram(s))	QD	Y-M: 20[redacted]
TORASEMIDE	5.0 mg (milligram(s))	QD	Y-M: 20[redacted]
MESALAZINE	1.0 g (gram(s))	TID	Y-M: 20[redacted]-[redacted] / -109
METHYLPREDNISOLONE	16.0 mg (milligram(s))	QD	Y-M: 20[redacted]-[redacted] / -28
FORTRANS	222.0 g (gram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -19
METAMIZOLE	2.0 g (gram(s))	Other: ONCE	Y-M: 20[redacted]-[redacted] / -18
PROPOFOL	120.0 mg (milligram(s))	Other: ONCE	Y-M: 20[redacted]-[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
BISOPROLOL	2.5 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
LEVOTHYROXINE	100 mcg (microgram(s))	QD	Y-M: 20[redacted]	ONGOING
TORASEMIDE	5.0 mg (milligram(s))	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	1.0 g (gram(s))	TID	Y-M: 20[redacted]-[redacted] / -109	Y-M: 20[redacted]-[redacted] / 298
MELOXICAM	15 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 268	Y-M: 20[redacted]-[redacted] / 277
SILYBUM MARIANUM	140 mg (milligram(s))	TID	Y-M: 20[redacted]-[redacted] / 298	Y-M: 20[redacted]-[redacted] / 313
DEXLANSOPRAZOLE	60 mg (milligram(s))	BID	Y-M: 20[redacted]-[redacted] / 305	Y-M: 20[redacted]-[redacted] / 308

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

Event Description	CHOLEDOCHOLITHIASIS
Preferred term	胆管結石
AE Onset Date / Rx Day	[redacted]20[redacted] / 278
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 278): ALANINE AMINO TRANSFERASE (SGPT/ALT): 336 [33 - 33] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 83 [32 - 32] U/L; CREATINE PHOSPHOKINASE: 892 [167 - 167] U/L; [redacted]20[redacted] (RX DAY 296): ALANINE AMINO TRANSFERASE (SGPT/ALT): 790 [10 - 31] U/L; ALKALINE PHOSPHATASE: 333 [45 - 129] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 439 [10 - 31] U/L; GAMAGLUTAMYLTRANSPEP: 938 [5 - 61] U/L; TOTAL BILIRUBIN: 30 [3 - 22] MCMOL/L; [redacted]20[redacted] (RX DAY 300): ALANINE AMINO TRANSFERASE (SGPT/ALT): 669 [0 - 55] U/L; ALKALINE PHOSPHATASE: 381 [40 - 150]

U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 547 [0 - 37] U/L; GGTP: 1027 [9 - 36] U/L; TOTAL BILIRUBIN: 31 [3 - 21] MCMOL/L; [redacted]20[redacted] (RX DAY 308): ALANINE AMINO TRANSFERASE (SGPT/ALT): 362 [7 - 56] U/L; ALKALINE PHOSPHATASE: 337 [38 - 126] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 108 [5 - 40] U/L; GGTP: 650 [7 - 50] U/L

Microbiology

[redacted]20[redacted] (RX DAY 300): Blood ANTY HCV: N; Blood HBSAG: N; Blood CMV-IGM: N; Blood ANTY HBS: N

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 296): USG SCAN OF ABDOMEN: LIVER IS NORMAL.STATUS AFTER CHOLECYSTECTOMY.COMMON BIL DUCT 7-8 MM, HEPATIC DUCTS NON DILATED. FEATURES OF AEROCHOLIA IN THE LEFT LIVER LOBE.PANCREAS NORMAL. WIRSUNG DUCT NON DILATED.SPLEN NORMAL. RE; [redacted]20[redacted] (RX DAY 305): ABDOMEN MRI WITH CONTRAST MEDIUM: LEFT HEPATIC DUCT:9MM, RIGHT HEPATIC DUCT 6MM., DILATED COMMON HEPATIC DUCT AND COMMON BIL DUCT TO 15MM., IN THE OSTIUM OF COMMON BIL DUCT SUGESTION OF BILE STONE 7MM; [redacted]20[redacted] (RX DAY 308): ENDOSCOPIC RETROGARD CGOLANGIOPANCEATOGR: ENDOSCOP INSERTED INTO DUODENUM. PAPILLA VATERI (MAJOR)WAS SWOLLEN. PHISICIAN　CANULLATED AND INJECTED CONTRAST MIDIUM INTO THE DILATATED BILE DUCTS WITH THE SHADOW OF A STONE. AFTER SPHINCTEROTOMY, B

AE Stopped Rx Day	308 (14 DAYS AFTER LAST TREATMENT)
Duration of AE	31 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	BILE LITHOGENICITY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の総胆管結石症が認められた。関連する病歴は，高血圧，閉経，胆嚢切除，及び左側潰瘍性大腸炎であった。被験者は非喫煙者及び非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，総胆管結石症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，総胆管結石症は回復した。

肝酵素活性の上昇及び腹痛が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は総胆管結石症のため入院した。臨床検査及び診断検査が実施された。内視鏡的逆行性胆道膵管造影（以下「ERCP」）検査及び乳頭括約筋切開術（以下「EPT」）が実施され，10 mm の結石が摘出された。ERCP 検査，EPT，及び結石摘出の後，症状が改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療薬として Legalon が投与された。

The patient's past medications include:

METYPRED for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [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 HUMIRA 40MG/0.8ML (Blinded)

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1) Choledocholithiasis (10049891) (Bile duct stone (10004637)) [v.22.0] [10049891]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of CHOLEDOCHOLITHIASIS

- Investigator: Bile lithogenicity.

- AbbVie: Event more likely related to past medical history of cholecystectomy. It is known that recurrence of choledocholithiasis is still observed in a considerable number of patients following cholecystectomy. Additional risk factors include subject's age, gender and pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMEN MRI WITH CONTRAST MEDIUM: Left hepatic duct: 9mm, right hepatic duct 6mm, dilated common hepatic duct and common bile duct to 15mm, in the ostium of common bile duct suggestion of bile stone 7mm

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 333 U/L (normal 45 to 129)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 381 U/L (normal 40 to 150)

[redacted] 20[redacted] ALKALINE PHOSPHATASE: 337 U/L (normal 38 to 126)

[redacted] 20[redacted] ANTY HBS: Negative

[redacted] 20[redacted] ANTY HCV: Negative

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

[redacted] 20[redacted] CREATINE PHOSPHOKINASE: 892 U/L (normal 167 to 167)

[redacted] 20[redacted] GAMAGLUTAMYLTRANSPEP: 938 U/L (normal 5 to 61)

[redacted] 20[redacted] GAMAGLUTAMYLTRANSPEP: 1027 U/L (normal 9 to 36)

[redacted] 20[redacted] GGTP: 650 U/L (normal 7 to 50)

[redacted] 20[redacted] HBSAG: Negative

[redacted] 20[redacted] SGOT/AST: 108 U/L (normal 5 to 40)

[redacted] 20[redacted] SGPT/ALT: 336 U/L (normal 33 to 33)

[redacted] 20[redacted] SGPT/ALT: 790 U/L (normal 10 to 31)

[redacted] 20[redacted] SGPT/ALT: 669 U/L (normal 0 to 55)

[redacted] 20[redacted] SGPT/ALT: 362 U/L (normal 7 to 56)

[redacted] 20[redacted] SGPT/AST: 83 U/L (normal 32 to 32)

[redacted] 20[redacted] SGPT/AST: 439 U/L (normal 10 to 31)

[redacted] 20[redacted] SGPT/AST: 547 U/L (normal 0 to 37)

[redacted] 20[redacted] TOTAL BILIRUBIN: 1.74 mg/dL (normal 0.20 to 1.30)

[redacted] 20[redacted] TOTAL BILIRUBIN: 1.8 mg/dL (normal 0.20 to 1.2)

[redacted] 20[redacted] USG SCAN OF ABDOMEN: Liver is normal status after cholecystectomy. Common bile duct 7-8 mm, hepatic ducts non dilated. Features of aerocholia in the left liver lobe. Pancreas normal. Wirsung duct non dilated. Spleen normal. Rens, bladder aorta, near aorta area: normal

Subject [redacted] (Investigator [redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	3[redacted]	MALE	White

Medical History	Onset Year
Not reported.	

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 45	45
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 56	[redacted]20[redacted] / 354	299

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	75 mg (milligram(s))	Other: 50 MORNING 25 EVENING	Y-M: 20[redacted]
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -338
POTASSIUM	1 CAPSUL	BID	Y-M: 20[redacted] / -41
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -40
FORTRANS	222 g (gram(s))	QD	Y-M: 20[redacted] / -10

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -338	ONGOING
POTASSIUM	1 CAPSUL	BID	Y-M: 20[redacted] / -41	ONGOING
BUDESONIDE	9 mg (milligram(s))	Other: EVERY OTHER DAY	Y-M: 20[redacted] / 36	ONGOING
TACROLIMUS	1 APPLICATION	TID	Y-M: 20[redacted] / 76	ONGOING
CIPROFLOXACIN	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 90
METRONIDAZOLE	500 mg (milligram(s))	BID	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 90
IBUPROFEN	200 mg (milligram(s))	TID	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 91

Event #1: Serious Adverse Event

Event Description	ACUTE APPENDICITIS
Preferred term	虫垂炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 83
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 84): SURGICAL INTERVENTION:APPENDECTOMY: APPENDECTOMY, PATIENT AFTER OPERATION: RECOVERING	
AE Stopped Rx Day	86
Duration of AE	4 DAYS
Severity	Severe

Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	[redacted]/20[redacted] ACUTE PAIN IN DOWN RIGHT PART OF ABDOMEN, WITH NUSEA AND VOMITTING, FEVER TO 39.0 DEGREE OF CELSIUS, HOSPITALIZED [redacted]/20[redacted], SURGICAL PROCEDURE: APPENDECTOMY WAS PERFORMED.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の急性虫垂炎が認められた。関連する病歴は，潰瘍性大腸炎（extensive colitis［脾彎曲部より口側に炎症が波及］）であった。被験者は非喫煙者及び非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，急性虫垂炎が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，急性虫垂炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日より，悪心及び嘔吐を伴う右下腹部の急性疼痛がみられ始め，最高で 39.0°C の発熱がみられた。20[redacted] 年 [redacted] 月 [redacted] 日，腹痛，悪心，嘔吐，及び発熱がみられ，被験者は急性虫垂炎と診断されて入院した。20[redacted] 年 [redacted] 月 [redacted] 日，虫垂切除術が実施された。被験者は回復していった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてメトロニダゾール，Ibuprom（イブプロフェン），及び Cipronex（シプロフロキサシン）が投与された。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Acute appendicitis (10000677) (Appendicitis (10003011)) [v.21.0] [10000677]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of ACUTE APPENDICITIS

- Investigator: [redacted] 20[redacted]: Acute pain in lower right part of abdomen with nausea and vomiting, fever to 39.0 degree of Celsius, hospitalized. [redacted] 20[redacted]: Surgical procedure, appendectomy was performed.

- AbbVie: Event is a common complication in the general population and is seen in up to 1 in 10 individuals over a lifetime. (Martin, RF. Acute Appendicitis in Adults: Diagnositic Evaulation In: Uptodate, Post TW (ED), Uptodate, Waltham, MA. (Accessed on [redacted], 20[redacted])).

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
リニア IgA 病	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY OTHER WEEK	6[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: MENOPAUSE	19[redacted]
ASTHMA	20[redacted]
CHOLECYSTITIS: CHOLECYSTECTOMY	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACKS	20	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB HIGHER INDUCTION DOSE	160/160/160/160/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44

ADALIMUMAB 4040 MG MG EVERY OTHER WEEK	EOW	[redacted]20[redacted] / 58	[redacted]20[redacted] / 220	163

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MONTELUKAST	4 mg (milligram(s))	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted]
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -300
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -234
FORTRANS	222 g (gram(s))	QD	Y-M: 20[redacted] / -7
METAMIZOLE	2 g (gram(s))	QD	Y-M: 20[redacted] / -6
PROPOFOL	140 mg (milligram(s))	QD	Y-M: 20[redacted] / -6

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MONTELUKAST	4 mg (milligram(s))	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 228
BUDESONIDE	9 mg (milligram(s))	QD	Y-M: 20[redacted] / -300	ONGOING
MESALAZINE	1 g (gram(s))	TID	Y-M: 20[redacted] / -234	ONGOING
PIMAFUCORT	1 TOPICAL	BID	Y-M: 20[redacted] / 108	ONGOING
METHYLPREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 170	Y-M: 20[redacted] / 206
METHYLPREDNISOLONE	18 mg (milligram(s))	QD	Y-M: 20[redacted] / 207	Y-M: 20[redacted] / 213
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] / 214	Y-M: 20[redacted] / 220
METHYLPREDNISOLONE	14 mg (milligram(s))	QD	Y-M: 20[redacted] / 221	Y-M: 20[redacted] / 225
CALCIUM CARBONATE	1 g (gram(s))	QD	Y-M: 20[redacted] / 226	ONGOING
METAMIZOLE	1 TABL	PRN	Y-M: 20[redacted] / 226	ONGOING
BILASTINE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 228

CLINDAMYCIN	1 DOSE	BID	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 228
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 228
POTASSIUM	1 TABL	QD	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 228
BUDESONIDE W/FORMOTEROL FUMARATE	80 mcg (microgram(s))	QD	Y-M: 20[redacted] / 229	ONGOING
DESLORATADINE	5 mg (milligram(s))	BID	Y-M: 20[redacted] / 229	ONGOING
MONTELUKAST	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 229	ONGOING
POTASSIUM	1 TABL	QD	Y-M: 20[redacted] / 229	ONGOING
SALBUTAMOL	100 mcg (microgram(s))	PRN	Y-M: 20[redacted] / 229	ONGOING
METHYLPREDNISOLONE	14 mg (milligram(s))	QD	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 229
METHYLPREDNISOLONE	40 mg (milligram(s))	QD	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 232
ACICLOVIR	500 mg (milligram(s))	TID	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 235
PARAFFIN, LIQUID	1 TOPICAL	QD	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 240
CLOBETASOL	1 DOSE	QD	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 247
METHYLPREDNISOLONE	16 mg (milligram(s))	QD	Y-M: 20[redacted] / 230	ONGOING
ATORVASTATIN	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 231	ONGOING
DAPSONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 233
METHYLPREDNISOLONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 235
DAPSONE	50 mg (milligram(s))	QD	Y-M: 20[redacted] / 234	ONGOING
CETIRIZINE	10 mg (milligram(s))	BID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 240

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

Event Description	LINEAR IGA BULLOUS DERMATOSIS
Preferred term	リニア IgA 病

AE Onset Date / Rx Day	[redacted]20[redacted] / 223 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 229): ANA: 320 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; ANA: 640 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 231): CHOLESTEROL: 6.16 [0 - 4.91] MMOL/L; CRP: 10.35 [0 - 9] MG/L; LDL CHOLESTEROL: 3.98 [0 - 2.97] MMOL/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 230): CHEST X RAY: NORMAL; SKIN BIOPSY: IGA+IGG DERMATOSIS; [redacted]20[redacted] (RX DAY 232): ABDOMEN ULTRASONOGRAPHY: NORMAL	
AE Stopped Rx Day	240 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	18 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の女性（ポーランド）であり，重篤な有害事象のリニア IgA 水疱性皮膚症が認められた。関連する病歴は，閉経，喘息，及び潰瘍性大腸炎であった。被験者は元喫煙者（1 日当たり 1 箱，喫煙期間 20 年）であり，断酒していた。

20[redacted] 年 [redacted] 月 [redacted] 日，リニア IgA 水疱性皮膚症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，リニア IgA 水疱性皮膚症は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，IgA 皮膚症が認められ，被験者は入院した。全身の皮膚が変色し，スティーヴンス・ジョンソン症候群が疑われた。20[redacted] 年 [redacted] 月 [redacted] 日，生検の結果により IgA/IgG 皮膚症の診断が確定された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Calperos，Kaldyum，Clatra（ビラスチン），Clindacne，Solu-Medrol（メチルプレドニゾロンコハク酸エステルナトリウム），Dapsone（ジアフェニルスルホン），

Hydrocortisonum，Cholesterol unguetum，Zyrtec（セチリジン塩酸塩），Hitaxa（デスロラタジン），Metypred（メチルプレドニゾロンコハク酸エステルナトリウム），Pyralginum，及びDermovate（クロベタゾールプロピオン酸エステル）が投与された。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Linear IgA bullous dermatosis (10048601) (Linear IgA disease (10024515)) [v.22.0] [10048601]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of LINEAR IGA BULLOUS DERMATOSIS

- Investigator: NOT APPLICABLE

- AbbVie: Formal studies validating the existence of drug-induced LABD are lacking. Additional RF includes UC. (Hall, Russell, et al. Linear IgA bullous dermatosis. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on [redacted] 20[redacted].))

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMEN ULTRASONOGRAPHY: Normal

[redacted] 20[redacted] ANA: 320 no unit

[redacted] 20[redacted] ANA: 640 no unit

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

[redacted] 20[redacted] CHOLESTEROL: 238 mg/dL (normal 0 to 190)

[redacted] 20[redacted] CRP: 10.35 MG/L (normal 0 to 9)

[redacted] 20[redacted] LDL CHOLESTEROL: 154 mg/dL (normal 0 to 115)

[redacted] 20[redacted] SKIN BIOPSY: IGA+IGG dermatosis

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
処置後出血	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB TDM	2[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: GENITOURINARY MALFORMATION	19[redacted]
OTHER: RIGHT OVARII CYST	20[redacted]
SURGERY: GENITOURINARY MALFORMATION	20[redacted]
CARDIAC ARRHYTHMIA: ATRIAL FIBRILLATION	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 49	49

ADALIMUMAB TDM	40/40/40/40 MG	EOW/EOW/EOW/EOW	[redacted]20[redacted] / 57[redacted]20[redacted] / 358		302

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	32 mg (milligram(s))	QD	Y-M: 20[redacted] / -132
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -49
MESALAZINE	1 g (gram(s))	QD	Y-M: 20[redacted] / -49
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / -49
POSTERISAN F	1 application	QD	Y-M: 20[redacted] / -49
FORTRANS	222 g (gram(s))	QD	Y-M: 20[redacted] / -15
METAMIZOLE	2 g (gram(s))	QD	Y-M: 20[redacted] / -14
PROPOFOL	160 mg (milligram(s))	QD	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
AZATHIOPRINE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -49	ONGOING
MESALAZINE	1 g (gram(s))	QID	Y-M: 20[redacted] / -49	ONGOING
METAMIZOLE	2 g (gram(s))	QD	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 365
PROPOFOL	160 mg (milligram(s))	QD	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 365

Event #1: Serious Adverse Event

Event Description	DIGESTIVE TRACT BLEEDING AFTER POLYPECTOMY
Preferred term	処置後出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 368 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 369): ALANINE AMINO TRANSFERASE (SGPT/ALT): 11 [7 - 56] U/L; AMYLASIS: 45 [1 - 100] U/L; ASPARTATE AMINO TRANSFERASE (SGOT/AST): 34 [5 - 40] U/L; BUN: 13.2 [5.4 - 17.1] MMOL/L; CREATININE: 58 [44 - 97] MCMOL/L; FERRITIN: 54 [13 - 150] NG/ML; FERRUM: 115 [37 - 158] MCG/DL; HEMATOCRIT: 0.27 [0.37 - 0.47] FRACTION; HEMOGLOBIN: 92 [120 - 160] G/L; HIGH-SENSITIVITY C-REACTIVE PROTEIN: 0.3 [0 - 10] MG/L; PLATELET COUNT: 177 [150 - 400] X10^9/L; RED BLOOD COUNT: 2.9 [3.8 - 5.2] X10^12/L; WHITE BLOOD COUNT: 8 [4 - 11] X10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted](RX DAY 368): X-RAY: NO EVIDENCE OF PERFORATION AND OBSTRUCTION OF THE GASTROINTESTINAL TRACT; USG: LIVER, PANCREAS,SPLEEN, AORTIS, ADRENAL GLANDS - NORMAL, KIDNEY - NORMAL, TRACE OF FLUID IN THE PERITONEUM IN THE LOWER ABDOMEN, NO THICKENING OF THE INTESTINAL WALLS; [redacted]20[redacted] (RX DAY 371): COLONOSCOPY: ULCERATION IN PLACE AFTER POLYPECTOMY

AE Stopped Rx Day	371 (13 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	NO
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（ポーランド）であり，重篤な有害事象のポリープ切除術後の消化管出血が認められた。関連する病歴は，心房細動及び左側潰瘍性大腸炎であった。被験者は非喫煙者及び非アルコール摂取者であった。
20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な左結腸曲のポリープが認められた。
20[redacted] 年 [redacted] 月 [redacted] 日，ポリープ切除術後の消化管出血が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，ポリープ切除術後の消化管出血は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，ポリープ切除術後の消化管出血が認められ，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，大腸内視鏡検査が実施された結果，ポリープ切除術後の潰瘍形成が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

METYPRED for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PENTASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

POSTERISAN H for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Post procedural bleeding (10051014) (Post procedural haemorrhage (10051077)) [v.22.0] [10051014]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of DIGESTIVE TRACT BLEEDING AFTER POLYPECTOMY

- Investigator: No.

- AbbVie: Event more likely related to polypectomy procedure. Pre-existing ulcerative colitis is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ENDOSCOPY: Not reported

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB 40 MG EVERY WEEK	2[redacted]	FEMALE	White

Medical History	Onset Year
OTHER: CUSHINGOID FACE AND NECK	20[redacted]
OTHER: SWOLLEN LOWER LIMBS	20[redacted]
PERIPHERAL ARTHROPATHY: SWOLLEN AND PAINFUL KNEE JOINTS	20[redacted]

Prior Procedures	Procedure Year
Colonoscopy	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB STANDARD INDUCTION DOSE	160/0/80/0/40 MG	EW/EW/EW/EW/EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 29	29
ADALIMUMAB 40 MG EVERY WEEK	40 MG	EW	[redacted]20[redacted] / 57	[redacted]20[redacted] / 316	260

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
IRON	2 DF (dosage form)	BID	Y-M: 20[redacted]
MESALAZINE	1.5 g (gram(s))	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg (milligram(s))	BID	Y-M: 20[redacted]
MERCAPTOPURINE	50 mg (milligram(s))	QD	Y-M: 20[redacted]
HYDROCORTISONE	100 mg (milligram(s))	QD	Y-M: 20[redacted] / -115
LEKOVIT CA	1 DF (dosage form)	QD	Y-M: 20[redacted] / -115
MESALAZINE	4 g (gram(s))	QD	Y-M: 20[redacted] / -115
METHYLPREDNISOLONE	32 mg (milligram(s))	QD	Y-M: 20[redacted] / -115
FORTRANS	148 g (gram(s))	QD	Y-M: 20[redacted] / -15
ETOMIDATE	3 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
METAMIZOLE	400 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
PROPOFOL	110 mg (milligram(s))	QD	Y-M: 20[redacted] / -14
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / -12

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
IRON	2 DF (dosage form)	BID	Y-M: 20[redacted]	ONGOING
MESALAZINE	1.5 g (gram(s))	BID	Y-M: 20[redacted]	ONGOING
LEKOVIT CA	1 DF (dosage form)	QD	Y-M: 20[redacted] / -115	ONGOING
LOPERAMIDE	2 mg (milligram(s))	PRN	Y-M: 20[redacted] / -12	Y-M: 20[redacted] / 315
ACETYLSALICYLIC ACID	75 mg (milligram(s))	QD	Y-M: 20[redacted] / 210	Y-M: 20[redacted] / 310
PROCTO HEMOLAN PROTECT	1 DF (dosage form)	BID	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 260
HYALURONIC ACID	1 DF (dosage form)	BID	Y-M: 20[redacted] / 261	ONGOING
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 261	Y-M: 20[redacted] / 267
METRONIDAZOLE	1 DF (dosage form)	QD	Y-M: 20[redacted] / 261	Y-M: 20[redacted] / 271
PREDNISONE	25 mg (milligram(s))	QD	Y-M: 20[redacted] / 268	Y-M: 20[redacted] / 281
PREDNISONE	20 mg (milligram(s))	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 295

PREDNISONE	15 mg (milligram(s))	QD	Y-M: 20[redacted] / 296	Y-M: 20[redacted] / 310
PREDNISONE	30 mg (milligram(s))	QD	Y-M: 20[redacted] / 311	Y-M: 20[redacted] / 338
BENZYDAMINE	1 DF (dosage form)	BID	Y-M: 20[redacted] / 314	Y-M: 20[redacted] / 322
KETAMINE	10 mg (milligram(s))	QD	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
MIDAZOLAM	1 mg (milligram(s))	QD	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
PROPOFOL	70 mg (milligram(s))	QD	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323

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

Event Description	ULCERATIVE COLITIS AGGRAVATED
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 246
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 325): COLECTOMY WITH ILEOSTOMY: NOT COMPLICATED; REVERSAL OF ILEOSTOMY IN FUTURE	
AE Stopped Rx Day	325 (9 DAYS AFTER LAST TREATMENT)
Duration of AE	80 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Investigator Alternative Etiology	AGGRAVATION OF ULCERATIVE COLITIS AFTER CORTICOSTEROIDS WITHDRAWAL
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:02:12

Program Source Code [redacted]