被験者番号 [redacted]

Event #1 of 1 : Serious Adverse Event

Preferred term	子宮脱

治験責任医師からの報告。本被験者はチェコ共和国の 6[redacted] 歳女性であり，米国アッヴィ社の ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，子宮脱を発現した。

Event 1 の臨床経過：

関連する病歴は，子宮頸部妊娠，強直性脊椎炎，子宮下垂症，脂肪肝，クレアチニンキナーゼ増加，現喫煙者（紙巻タバコ 1 日 5 本を 48 年間）及び現飲酒者（1 日 2 杯未満）であった。

被験者は投与 14 週時までは盲検下で治験に参加していた。投与開始から 106 日後，被験者は第 2 ピリオドに移行し，ウパダシチニブの非盲検投与を開始した。

投与開始から 409 日後，被験者は子宮脱を発現した。投与開始から 463 日後，子宮脱は消失した。

投与開始から 462 日後，被験者は予定されていた外科手術のため入院した。投与開始から 463 日後，被験者は子宮摘出術及び卵巣摘出術を受け，合併症は認められなかった。外科手術は予防的なものであり，産婦人科医に推奨されたものであった。投与開始から 466 日後，被験者は退院した。

投与された薬剤は，ピリドキシンであった。

M19-944 試験 Study 1（14 週）

治験の標題：A Phase 3 Randomized, Placebo-Controlled, Double-Blind Program to Evaluate Efficacy and Safety of Upadacitinib in Adult Subjects with Axial Spondyloarthritis Followed by a Remission-Withdrawal Period	
施設数 / 実施国名： 119 施設 / アルゼンチン，オーストラリア，ブラジル，ブルガリア，カナダ，中国，チェコ，ドイツ，ハンガリー，イスラエル，日本，メキシコ，ニュージーランド，ポーランド，ロシア，韓国，スペイン，台湾，トルコ，ウクライナ，英国，米国（22 ヵ国）	
治験調整医師： [redacted], MD	
公表文献 (参考資料) ： なし	
治験期間： 最初の被験者の初回来院日：20[redacted] 年[redacted]月[redacted] 日 最後の被験者の最終来院日：20[redacted] 年[redacted] 月[redacted] 日	開発のフェーズ：III

目的：試験の目的は以下のとおりであった。

<u>二重盲検投与期：</u>

- 生物学的疾患修飾性抗リウマチ薬（以下「bDMARD」）で効果不十分な強直性脊椎炎患者（Study 1）及び X 線基準を満たさない体軸性脊椎関節炎（以下「nr-axSpA」）患者（Study 2）を含む活動性の体軸性脊椎関節炎（以下「axSpA」）の成人患者を対象に，徴候・症状の緩和におけるウパダシチニブの有効性をプラセボとの比較により評価する。
- bDMARD で効果不十分な強直性脊椎炎患者（Study 1）及び nr-axSpA 患者（Study 2）を含む活動性 axSpA の成人患者を対象に，ウパダシチニブの安全性及び忍容性を評価する。

<u>非盲検継続投与期：</u>

二重盲検投与期を終了した bDMARD で効果不十分な強直性脊椎炎患者（Study 1）及び二重盲検投与期を終了した nr-axSpA 患者（Study 2）を含む活動性 axSpA の成人患者を対象に，継続投与におけるウパダシチニブの安全性及び忍容性を評価する。

<u>寛解・投与中止期：</u>

投与 104 週時に強直性脊椎炎疾患活動性スコア（以下「ASDAS」）1.3 未満かつ投与 88 週時に ASDAS 2.1 未満を達成した患者を対象に，ウパダシチニブ中止後の疾患コントロールの維持を評価する。

被験者数（計画時と解析時）：
計画時：386 例，解析時：420 例

診断と主要な組入れ基準：
本試験には以下の被験者を組み入れた：

- 18 歳以上の男性又は女性
- 強直性脊椎炎と臨床的に診断され，強直性脊椎炎の改訂 New York Criteria を満たす患者
- 脊椎全強直が認められない患者
- スクリーニング来院及びベースライン来院時において，0–10 の数値化格付けスケールに基づくベースラインの疾患活動性が，バース強直性脊椎炎疾患活動性指標（以下「BASDAI」）スコア 4 以上及び全般背部痛の患者による評価スコア 4 以上の患者
- 治験責任（分担）医師によって，最大推奨用量若しくは最大耐量で 2 種類以上の非ステロイド系抗炎症薬（以下「NSAID」）の計 4 週間以上の投与を受けて効果不十分，又は NSAID に対して忍容性がなかった若しくは禁忌と判定された患者

- 1 又は 2 種類の bDMARD による治療歴があり，効果不十分又は忍容性がないことにより当該 bDMARD を中止した患者
- 腫瘍壊死因子（以下「TNF」）阻害剤及びインターロイキン（以下「IL」）-17 阻害剤の両方で効果不十分であった患者は不適格とした
- axSpA 以外の様々な原因による炎症性関節炎の既往歴がない患者

治験方法：

本試験は実施中の第 III 相多施設共同試験であり，bDMARD で効果不十分な強直性脊椎炎（Study 1）及び nr-axSpA（Study 2）を含む活動性 axSpA の患者を対象とする独立した 2 つの試験で構成される。M19-944 試験 Study 1 中間治験総括報告書（以下「CSR」）は，Study 1（bDMARD で効果不十分な強直性脊椎炎）に焦点を当てており，Study 2（nr-axSpA）については文脈上必要な場合にのみ記載した。

Study 1（bDMARD で効果不十分な強直性脊椎炎）は，35 日間のスクリーニング期間，14 週間のランダム化二重盲検並行群間プラセボ対照期間（二重盲検投与期），90 週間の非盲検長期継続投与期間（非盲検継続投与期）及び 30 日の追跡調査来院で構成される。

30 日の追跡調査来院では，継続中の有害事象 / 重篤な有害事象の状態又は新たな有害事象 / 重篤な有害事象の発生を判断するため，来院に代わって電話連絡を実施することが可能であり，これらの被験者は治験を完了したとみなした。

Study 1（bDMARD で効果不十分な強直性脊椎炎）の二重盲検投与期では，被験者を第 1 群：ウパダシチニブ 15 mg 1 日 1 回（193 例）又は第 2 群：プラセボ 1 日 1 回（193 例）のいずれかに 1：1 の比率でランダムに割り付けた。

プラセボ群の被験者は，投与 14 週時にウパダシチニブ 15 mg 1 日 1 回へ切り替え，非盲検継続投与期に移行した。

投与 104 週時に寛解状態にある被験者は，寛解・投与中止期に適格とした。投与 152 週時まで治験薬を投与せずに被験者を追跡し，疾患再燃の有無を評価した。再燃が認められた場合は，再燃が認められた時点から 24 週間（又は各国の要件によってはそれ以上の期間）にわたり非盲検でウパダシチニブ 15 mg 1 日 1 回投与（再投与）を行った。再燃が認められない場合は，ウパダシチニブを投与せずに投与 152 週時まで追跡した。投与 104 週時に寛解状態にない被験者については，30 日の追跡調査来院後に治験を終了するか，該当する場合は，各国の要件に基づく場合に限り，事前に規定した時点まで非盲検でウパダシチニブを投与することも可能とした。

M19-944 試験 Study 1 中間 CSR には，Study 1（bDMARD で効果不十分な強直性脊椎炎）の 14 週間のすべての結果を示した。有効性は投与 14 週時までのデータを示した。安全性及び被験者背景はカットオフ日（20[redacted] 年 [redacted] 月 [redacted] 日）までのデータを示し，14 週間のデータ及び入手可能なすべての長期投与データの要約を含めた。

被験薬，用量，投与方法及びバッチ番号：

ウパダシチニブ 15 mg 錠を 1 日 1 回，投与 1 日目（ベースライン）から毎日ほぼ同じ時刻に，食事を摂るタイミングに関わらず経口投与した。

治験薬	投与経路	剤形	用量	製造元	バッチ番号
ウパダシチニブ	経口	錠剤	15 mg	米国アッヴィ社	[redacted]

投与期間：Study 1（bDMARD で効果不十分な強直性脊椎炎）では 90 週間又は 104 週間（寛解・投与中止期の潜在的投与期間は含まない）

対照薬，用量，投与方法及びバッチ番号：
ウパダシチニブに対応するプラセボを 1 日 1 回，投与 1 日目（ベースライン）から毎日ほぼ同じ時刻に，食事を摂るタイミングに関わらず経口投与した。

治験薬	投与経路	剤形	用量	製造元	バッチ番号
ウパダシチニブに対応するプラセボ	経口	錠剤	該当せず	米国アッヴィ社	[redacted]

評価基準：

有効性：

本試験で収集した有効性評価項目は以下を含むがこれらに限定されない。

- 国際脊椎関節炎評価学会（以下「ASAS」）20 / 40 反応及び部分寛解（以下「PR」）を含む ASAS 反応
- ASDAS 非活動性疾患，ASDAS 低疾患活動性，ASDAS 大幅改善及び ASDAS 臨床的に重要な改善を含む ASDAS 及び ASDAS 反応
- BASDAI の 50%以上の改善（以下「BASDAI50」）を含む BASDAI 反応
- 全般背部痛の患者による評価（以下「全般背部痛」）
- 夜間背部痛の患者による評価（以下「夜間背部痛」）
- 疾患活動性の患者による全般的評価（以下「PtGA」）
- 疼痛の患者による全般的評価
- バース強直性脊椎炎疾患機能指標（以下「BASFI」）
- Ankylosing Spondylitis Quality of Life（以下「ASQoL」）
- ASAS 健康指標（以下「HI」）
- 線形バース強直性脊椎炎疾患計測学指標（以下「$BASMI_{lin}$」）
- マーストリヒト強直性脊椎炎付着部炎スコア（以下「MASES」）
- 高感度 C 反応性たん白（以下「hsCRP」）
- 磁気共鳴画像法（以下「MRI」）カナダ脊椎関節炎研究コンソーシアム（以下「SPARCC」）スコア（脊椎及び仙腸［以下「SI」］関節）
- レスキュー治療の開始
- 修正ストーク強直性脊椎炎脊椎スコア（以下「mSASSS」）
- EuroQoL-5D-5L（以下「EQ-5D-5L」）
- 慢性疾患療法の機能的評価－倦怠感（以下「FACIT-F」）
- NSAID スコア
- オピオイドの使用
- 装着可能な機器による身体活動量評価
- 疾患活動性の医師による全般的評価
- 36 項目 Short Form 健康調査（以下「SF-36」）
- 圧痛関節数及び腫脹関節数
- 再燃までの期間
- 仕事の生産性及び活動障害（以下「WPAI」）

薬物動態：

ベースライン後の所定の治験来院時に血漿中ウパダシチニブ測定用の採血を実施した。投与 2 週時と投与 8 週時の

来院時の採血は，可能であれば投与前に実施した。他のすべての来院については，来院中任意の時点で採血を実施した。

安全性：

安全性評価項目は，全試験期間をとおした安全性及び忍容性の評価として，有害事象モニタリング，身体検査，バイタルサイン測定及び臨床検査（血液学的検査，生化学検査及び尿検査）とした。心電図はスクリーニング時及び各国の要件に応じて年 1 回実施した。

統計手法：

有効性：

すべての被験者が 14 週間の二重盲検投与期を終了又は二重盲検投与期間中に早期中止し，データベースロックを行った後に主要解析を行った。プラセボと比較した 14 週間の有効性を示した。治験実施計画書で規定した主要な時点について，ランダム割付けされた治療群（ウパダシチニブ 15 mg 1 日 1 回群及びプラセボ群）ごとに解析を実施した。治験実施計画書で規定した治験薬の切り替えは，二重盲検投与期間中には発生しなかった。規定どおりの統計的推定を行い，この一連の解析結果を本試験の主要な有効性の結果とした。

すべての有効性解析は，最大の解析対象集団を対象として実施した。さらに，主要評価項目の解析は，治験実施計画書に適合した解析集団を対象として実施した。すべての解析は有意水準 $\alpha = 0.05$ の両側検定として実施した。「ベースライン」とは，治験薬初回投与前又は治験薬未投与の場合はランダム割付け前の，欠測でない最後の観察項目を指す。プラセボと比較した 14 週間の有効性を示した。

2 値変数に関するウパダシチニブ群とプラセボ群の比較は，層別因子であるスクリーニング時の hsCRP 値で調整した（基準値上限［以下「ULN」］超又は ULN 以下）Cochran-Mantel-Haenszel 検定を用いて行った。連続変数に関するウパダシチニブ群とプラセボ群の比較では，投与群，来院，及び来院と治療の相互作用を固定効果，対応するベースライン値を共変量として，スクリーニング時の hsCRP 値で調整した混合効果・反復測定モデルを用いた。

薬物動態：

被験者ごとの血漿中ウパダシチニブ濃度を表にまとめて要約した。

安全性：

安全性解析は安全性解析対象集団を対象として行った。安全性解析対象集団には，治験薬を 1 回でも投与されたすべての被験者を含めた。安全性はカットオフ日（20[redacted] 年 [redacted] 月 [redacted] 日）までのデータを示し，14 週間のデータ及び入手可能なすべての長期投与データの要約を含めた。安全性は，治験薬投与後に発現した有害事象（以下「TEAE」），臨床検査及びバイタルサインにより評価した。国際医薬用語集（以下「MedDRA」）の器官別大分類（以下「SOC」）及び基本語（以下「PT」）別に，有害事象（特に記載がない限り，すべての TEAE）を発現した被験者数及び割合（%）を投与群ごとに表にまとめた。また，重篤な有害事象，重症度別の有害事象，及び治験責任（分担）医師が評価した治験薬との因果関係別有害事象の要約を示した。重篤な有害事象及び治験中止に至った有害事象を一覧に示した。各来院時におけるバイタルサイン及び臨床検査値を要約した。特定の臨床検査値について，ベースラインからの変化量を要約した。臨床検査値のベースラインから規定された時点までの変動を表に示した。

要約 / 結論

有効性の結果：

本試験では，2 種類以上の NSAID で効果不十分（又は NSAID に対して忍容性がないか禁忌）及び bDMARD（TNF 阻害剤又は IL-17 阻害剤）による治療で効果不十分であった強直性脊椎炎の被験者における，ウパダシチニブ 15 mg 錠 1 日 1 回投与の有効性をプラセボと比較して評価した。投与 14 週時に ASAS40 反応が得られた被験者の割合は，プラセボ群 18.2%に対してウパダシチニブ群は 44.5%であり統計学的に有意に高かったことから，本試験の主要評価項目を達成した。ウパダシチニブの効果の迅速な発現は，ASAS40 及び個々の構成要素の大部分において一貫して認められ，全般背部痛，PtGA 及び炎症については 1 週以降，BASFI については 4 週以

降に認められた。さらに，ASAS40 反応は，1 種類の TNF 阻害剤への曝露歴がある被験者及び 1 種類の IL-17 阻害剤への曝露歴がある被験者も含め，事前に規定した部分集団のすべてにおいてプラセボ群と比較してウパダシチニブ群で一貫して高かった。

加えて，本試験では，疾患活動性の改善（C 反応性たん白［以下「CRP」］に基づく ASDAS，ASDAS 非活動性疾患，ASDAS 低疾患活動性，BASDAI50，ASAS20 及び ASAS PR），疼痛（全般背部痛及び夜間背部痛），機能指標（BASFI），炎症（SPARCC スコア［脊椎］），生活の質（以下「QoL」）（ASQoL 及び ASAS HI），脊椎可動性（$BASMI_{lin}$）及び付着部炎（MASES）を含む，投与 14 週時における多重性を調整した副次評価項目をすべて達成した。

投与 14 週時に MRI SPARCC スコア（SI 関節）の改善及び臨床的に関連のある ASDAS 反応（ASDAS 大幅改善及び ASDAS 臨床的に重要な改善）を示した被験者の割合は，プラセボを投与された被験者と比較してウパダシチニブを投与された被験者で一貫して高かった。

全般背部痛と夜間背部痛の改善を補完するものとして，他の部位の背部痛（首，腰，背中など），末梢痛，及び疼痛の全般的評価についても，プラセボ群と比較してウパダシチニブ群で一貫した迅速な改善が認められた。

投与 14 週時の健康関連 QoL（EQ-5D-5L 及び SF-36），倦怠感（FACIT-F 及び BASDAI 質問 1）及び仕事の生産性（WPAI）の改善は，プラセボを投与された被験者と比較してウパダシチニブを投与された被験者で大きかった。

薬物動態の結果：

ウパダシチニブ 15 mg 1 日 1 回を投与した被験者における投与後 24 時間以内のウパダシチニブの平均血漿中濃度は，6.99 ng/mL から 23.5 ng/mL の範囲であった。この結果は，ウパダシチニブを用いた試験で以前に認められたウパダシチニブの薬物動態と一致した。

安全性の結果：

Study 1（bDMARD で効果不十分な強直性脊椎炎）の二重盲検投与期及び利用可能な長期の安全性の結果は，重篤な有害事象，治験薬の投与中止に至った有害事象及び特に注目すべき有害事象を含む有害事象の発現頻度，並びに臨床検査データ及びバイタルサインの評価から，ウパダシチニブ 15 mg 1 日 1 回経口投与の忍容性はおおむね良好であることが示された。この結果は，関節リウマチ，関節症性乾癬，及び bDMARD 未使用の強直性脊椎炎のウパダシチニブ臨床試験で観察された結果と一致するものであった。Study 1（bDMARD で効果不十分な強直性脊椎炎）でウパダシチニブ投与群の被験者において報告された有害事象の大部分は，強直性脊椎炎の患者集団で予想されるもの，又はウパダシチニブを含むヤヌスキナーゼ阻害剤の添付文書に既に記載されているものと一致していた。

二重盲検投与期に重篤な有害事象を発現した被験者の割合は，プラセボ群と比較してウパダシチニブ群で高かった。ウパダシチニブ群で重篤な有害事象を発現した 6 例中 4 例が新型コロナウイルス感染症（以下「COVID-19」）関連の重篤な有害事象を発現しており，現在進行中の COVID-19 パンデミックを反映するものであった。長期投与データで発現した 28 件の重篤な有害事象のうち，COVID-19 関連の重篤な有害事象は 10 件であった。COVID-19 関連の重篤な有害事象のうち，治験責任（分担）医師により治験薬と関連ありと判断されたものはなかった。

非盲検継続投与期に 1 例の被験者が高所からの転落による多発性外傷により死亡した。警察の報告書では本事象は自殺とされており，治験責任（分担）医師は治験薬と関連なしと判断した。

報告された重篤な感染症の大部分は COVID-19 又は COVID-19 肺炎であった。重篤な感染症のうち，ウパダシチニブの投与中止に至ったものはなかった。長期投与データでの帯状疱疹の発現率は 4.1 件 / 100 人年であり，これらの事象は治験責任（分担）医師により治験薬と関連ありと判断された。1 件を除くすべての帯状疱疹は軽度又は中等度であり，非重篤であった。糖尿病の既往歴のある日本人の被験者 1 例に重篤な播種性水痘帯状疱疹ウイルス感染が認められたが，皮膚外臓器の病変は認められなかった。

データカットオフ日までに，ウパダシチニブを投与された 1 例が非致死性の静脈血栓塞栓症である肺塞栓症を 1 件発現した。本事象は，治験責任（分担）医師により，重度で，生命を脅かす重篤な有害事象であり，治験薬と関連ありと判断された。他の 1 例の被験者は右鼻の基底細胞癌と診断され，これにより治験薬は休薬となった。

本事象は，治験責任（分担）医師により，軽度であり，治験薬と関連なしと判断された。ウパダシチニブを投与された被験者において，非黒色腫皮膚癌以外の悪性腫瘍，消化管穿孔，腎機能障害，日和見感染（結核及び帯状疱疹を除く），活動性結核及び主要心血管系事象と評価判定された事象の有害事象は報告されなかった。

長期投与データで関節外症状の発生率は低く，ぶどう膜炎は 1.5 件 / 100 人年，炎症性腸疾患は 0.4 件 / 100 人年であった。これらの事象のうち治験薬の投与中止に至ったものはなかった。

二重盲検投与期及び非盲検継続投与期の大部分の血液学的検査及び生化学検査パラメータに関して，ベースライン時のグレード 0 から，ベースライン後の最悪値でグレード 2 又は 3 に移行した被験者は少なく，グレード 4 に移行した被験者はいなかった。いずれのパラメータにおいても，グレード 0 からグレード 3 に移行した被験者は 2%未満であった。肝機能に関連する臨床検査値の変化で報告頻度が高かった事象は，アラニンアミノトランスフェラーゼ（以下「ALT」）の ULN の 3 倍以上の上昇（3.0%）及びアスパラギン酸アミノトランスフェラーゼ（以下「AST」）の ULN の 3 倍以上の上昇（3.6%）であった。なお，二重盲検投与期間中にウパダシチニブ群の 1 例で，ALT 及び AST の ULN の 3 倍以上の上昇と総ビリルビンの ULN の 2 倍以上の上昇が同時に起こったが，これらの値は急性胆管炎の重篤な有害事象において発現したものであり，確定した Hy's law のケースに該当するものではなかった。

二重盲検投与期及び非盲検継続投与期において，潜在的に臨床的に重要（以下「PCS」）な体重の変化（ベースラインから 7%超の減少又は増加）が認められた。データカットオフ日までに，ウパダシチニブを投与された被験者のうち 3.8%の被験者に PCS に該当する体重減少が認められ，11.2%の被験者に PCS に該当する体重増加が認められた。

bDMARD で効果不十分な強直性脊椎炎患者を対象とした本試験で観察された安全性プロファイルは，全体的にウパダシチニブの既知の知見と一致しており，新たな安全性上のリスクは確認されなかった。

結論：

M19-944 試験 Study 1（bDMARD で効果不十分な強直性脊椎炎患者）で，bDMARD 療法で効果不十分な活動性強直性脊椎炎患者にウパダシチニブ 15 mg を 1 日 1 回経口投与したとき，疾患活動性，疼痛，機能指標，QoL，付着部炎，脊椎可動性，及び MRI で検出された体軸の炎症において，投与 14 週時にプラセボと比較して統計学的に有意な改善が示された。ウパダシチニブ 15 mg 1 日 1 回投与は概して安全であり，忍容性は良好であった。関連する関節リウマチ，関節症性乾癬及び強直性脊椎炎のプログラムで知られているウパダシチニブの既知の安全性プロファイルと比較して，新たな安全性上のリスクは認められなかった。本試験の結果は，bDMARD で効果不十分な活動性強直性脊椎炎患者に対するウパダシチニブ 15 mg 1 日 1 回投与の使用を支持するものであった。

表 1. 二重盲検投与期（投与 14 週時まで）における有害事象（MedDRA SOC 及び PT 別）（M19-944 試験，安全性解析対象集団）

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
Any adverse event	77 (36.8)	86 (40.8)
血液およびリンパ系障害	4 (1.9)	12 (5.7)
貧血	1 (0.5)	2 (0.9)
白血球増加症	0	1 (0.5)
白血球減少症	0	4 (1.9)
リンパ節症	1 (0.5)	0
リンパ球増加症	0	1 (0.5)
リンパ球減少症	1 (0.5)	1 (0.5)
好中球減少症	1 (0.5)	6 (2.8)
心臓障害	1 (0.5)	0
動悸	1 (0.5)	0
眼障害	5 (2.4)	2 (0.9)
眼瞼炎	0	1 (0.5)
結膜出血	1 (0.5)	0
ドライアイ	1 (0.5)	0
虹彩毛様体炎	1 (0.5)	0
ぶどう膜炎	2 (1.0)	1 (0.5)
胃腸障害	15 (7.2)	17 (8.1)
腹部不快感	1 (0.5)	0
腹部膨満	0	2 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
胃腸障害 (Cont.)		
腹痛	2 (1.0)	1 (0.5)
上腹部痛	1 (0.5)	2 (0.9)
アフタ性潰瘍	0	2 (0.9)
慢性胃炎	0	1 (0.5)
クローン病	0	1 (0.5)
下痢	5 (2.4)	3 (1.4)
消化不良	2 (1.0)	0
鼓腸	1 (0.5)	0
食中毒	1 (0.5)	1 (0.5)
胃炎	0	2 (0.9)
痔出血	0	1 (0.5)
痔核	1 (0.5)	0
鼠径ヘルニア	1 (0.5)	0
口腔内潰瘍形成	1 (0.5)	1 (0.5)
悪心	2 (1.0)	0
閉塞性膵炎	1 (0.5)	0
嚥下痛	1 (0.5)	0
歯痛	0	1 (0.5)
嘔吐	1 (0.5)	1 (0.5)
一般・全身障害および投与部位の状態	8 (3.8)	5 (2.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
一般・全身障害および投与部位の状態 (Cont.)		
適用部位疼痛	1 (0.5)	0
無力症	1 (0.5)	0
胸痛	1 (0.5)	0
疲労	1 (0.5)	4 (1.9)
インフルエンザ様疾患	1 (0.5)	0
倦怠感	1 (0.5)	0
疼痛	1 (0.5)	2 (0.9)
末梢腫脹	1 (0.5)	0
発熱	1 (0.5)	0
肝胆道系障害	0	1 (0.5)
急性胆管炎	0	1 (0.5)
免疫系障害	1 (0.5)	1 (0.5)
食物アレルギー	1 (0.5)	0
季節性アレルギー	0	1 (0.5)
感染症および寄生虫症	24 (11.5)	29 (13.7)
無症候性ＣＯＶＩＤ－１９	1 (0.5)	3 (1.4)
細菌性膣症	0	2 (0.9)
気管支炎	1 (0.5)	1 (0.5)
ウイルス性気管支炎	1 (0.5)	0
ＣＯＶＩＤ－１９	4 (1.9)	7 (3.3)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
感染症および寄生虫症 (Cont.)		
ＣＯＶＩＤ－１９肺炎	0	4 (1.9)
コクサッキーウイルス感染	0	1 (0.5)
膀胱炎	0	1 (0.5)
毛包炎	1 (0.5)	0
せつ	1 (0.5)	0
胃腸炎	1 (0.5)	0
消化管感染	1 (0.5)	0
泌尿生殖器感染	1 (0.5)	0
ヘリコバクター性胃炎	0	1 (0.5)
帯状疱疹	0	2 (0.9)
麦粒腫	0	1 (0.5)
上咽頭炎	3 (1.4)	5 (2.4)
咽頭炎	0	1 (0.5)
肺炎	0	1 (0.5)
歯髄炎	1 (0.5)	0
気道感染	1 (0.5)	1 (0.5)
鼻炎	1 (0.5)	0
副鼻腔炎	0	1 (0.5)
白癬感染	0	1 (0.5)
歯感染	1 (0.5)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
感染症および寄生虫症 (Cont.)		
上気道感染	4 (1.9)	2 (0.9)
尿路感染	2 (1.0)	0
ウイルス感染	1 (0.5)	0
ウイルス性咽頭炎	0	1 (0.5)
ウイルス性上気道感染	1 (0.5)	0
外陰部腟カンジダ症	1 (0.5)	0
傷害、中毒および処置合併症	3 (1.4)	6 (2.8)
節足動物咬傷	1 (0.5)	0
挫傷	0	2 (0.9)
転倒	0	1 (0.5)
関節損傷	1 (0.5)	0
靭帯断裂	1 (0.5)	0
半月板損傷	1 (0.5)	0
筋損傷	0	1 (0.5)
肉離れ	0	1 (0.5)
皮膚擦過傷	1 (0.5)	0
皮膚裂傷	0	1 (0.5)
臨床検査	7 (3.3)	11 (5.2)
アラニンアミノトランスフェラーゼ増加	1 (0.5)	3 (1.4)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.5)	3 (1.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
臨床検査 (Cont.)		
血中アルカリホスファターゼ増加	1 (0.5)	0
血中ブドウ糖増加	0	1 (0.5)
血圧異常	0	1 (0.5)
血中トリグリセリド増加	1 (0.5)	0
ヘモグロビン減少	0	1 (0.5)
肝酵素上昇	0	1 (0.5)
リンパ球数減少	1 (0.5)	0
好中球数減少	1 (0.5)	0
血小板数増加	0	1 (0.5)
トランスアミナーゼ上昇	1 (0.5)	1 (0.5)
尿潜血陽性	0	2 (0.9)
体重減少	2 (1.0)	0
体重増加	0	1 (0.5)
代謝および栄養障害	6 (2.9)	13 (6.2)
糖尿病	0	1 (0.5)
耐糖能障害	1 (0.5)	1 (0.5)
痛風	1 (0.5)	0
高コレステロール血症	0	1 (0.5)
高血糖	0	2 (0.9)
高カリウム血症	1 (0.5)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
代謝および栄養障害 (Cont.)		
高脂血症	1 (0.5)	1 (0.5)
高尿酸血症	0	5 (2.4)
低コレステロール血症	0	1 (0.5)
低カリウム血症	0	1 (0.5)
低ナトリウム血症	1 (0.5)	0
空腹時血中ブドウ糖不良	1 (0.5)	0
筋骨格系および結合組織障害	18 (8.6)	5 (2.4)
強直性脊椎炎	1 (0.5)	0
関節痛	8 (3.8)	0
関節炎	0	1 (0.5)
軸性脊椎関節炎	4 (1.9)	0
背部痛	4 (1.9)	1 (0.5)
肋軟骨炎	1 (0.5)	0
関節強直	1 (0.5)	0
関節硬直	1 (0.5)	0
関節腫脹	1 (0.5)	0
半月板変性	1 (0.5)	0
筋痙縮	0	1 (0.5)
筋緊張	0	1 (0.5)
四肢痛	2 (1.0)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
筋骨格系および結合組織障害 (Cont.)		
滑液嚢腫	1 (0.5)	0
滑膜炎	1 (0.5)	1 (0.5)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.5)	0
扁桃癌	1 (0.5)	0
神経系障害	8 (3.8)	10 (4.7)
味覚消失	0	1 (0.5)
手根管症候群	1 (0.5)	0
浮動性めまい	2 (1.0)	0
頭痛	3 (1.4)	7 (3.3)
感覚鈍麻	2 (1.0)	0
片頭痛	0	1 (0.5)
末梢性ニューロパチー	1 (0.5)	0
失神	0	1 (0.5)
精神障害	5 (2.4)	1 (0.5)
不安	1 (0.5)	0
不眠症	3 (1.4)	0
易刺激性	0	1 (0.5)
リビドー亢進	0	1 (0.5)
ストレス	1 (0.5)	0
腎および尿路障害	2 (1.0)	5 (2.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
腎および尿路障害 (Cont.)		
尿路結石	0	2 (0.9)
血尿	0	3 (1.4)
腎結石症	1 (0.5)	1 (0.5)
腎仙痛	1 (0.5)	0
生殖系および乳房障害	2 (1.0)	2 (0.9)
月経障害	1 (0.5)	0
卵巣嚢胞	1 (0.5)	0
骨盤痛	1 (0.5)	1 (0.5)
子宮ポリープ	1 (0.5)	0
腟嚢胞	0	1 (0.5)
呼吸器、胸郭および縦隔障害	5 (2.4)	2 (0.9)
咳嗽	1 (0.5)	0
鼻出血	1 (0.5)	0
喉頭出血	1 (0.5)	0
鼻閉	1 (0.5)	0
口腔咽頭痛	2 (1.0)	0
呼吸障害	0	2 (0.9)
皮膚および皮下組織障害	4 (1.9)	6 (2.8)
ざ瘡	0	2 (0.9)
脱毛症	0	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
皮膚および皮下組織障害 (Cont.)		
アレルギー性皮膚炎	1 (0.5)	0
接触皮膚炎	1 (0.5)	1 (0.5)
皮膚乾燥	1 (0.5)	0
斑状出血	0	1 (0.5)
そう痒症	0	1 (0.5)
乾癬	1 (0.5)	0
皮膚刺激	0	1 (0.5)
血管障害	4 (1.9)	0
高血圧	4 (1.9)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]
相互参照：M19-944試験 Study 1 中間CSR TABLE 14.3__1.2.1.1

表 2. 二重盲検投与期（投与 14 週時まで）における治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（M19-944 試験，安全性解析対象集団）

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
Any adverse event	25 (12.0)	36 (17.1)
血液およびリンパ系障害	2 (1.0)	11 (5.2)
貧血	0	1 (0.5)
白血球増加症	0	1 (0.5)
白血球減少症	0	4 (1.9)
リンパ球増加症	0	1 (0.5)
リンパ球減少症	1 (0.5)	1 (0.5)
好中球減少症	1 (0.5)	6 (2.8)
眼障害	0	1 (0.5)
眼瞼炎	0	1 (0.5)
胃腸障害	5 (2.4)	5 (2.4)
腹部膨満	0	1 (0.5)
腹痛	1 (0.5)	0
上腹部痛	1 (0.5)	1 (0.5)
アフタ性潰瘍	0	1 (0.5)
慢性胃炎	0	1 (0.5)
下痢	2 (1.0)	2 (0.9)
消化不良	1 (0.5)	0
悪心	1 (0.5)	0
嘔吐	1 (0.5)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
一般・全身障害および投与部位の状態	2 (1.0)	1 (0.5)
疲労	1 (0.5)	1 (0.5)
疼痛	1 (0.5)	0
感染症および寄生虫症	8 (3.8)	9 (4.3)
無症候性ＣＯＶＩＤ－１９	0	1 (0.5)
細菌性膣症	0	2 (0.9)
ウイルス性気管支炎	1 (0.5)	0
毛包炎	1 (0.5)	0
胃腸炎	1 (0.5)	0
泌尿生殖器感染	1 (0.5)	0
帯状疱疹	0	2 (0.9)
上咽頭炎	0	1 (0.5)
肺炎	0	1 (0.5)
歯髄炎	1 (0.5)	0
副鼻腔炎	0	1 (0.5)
上気道感染	2 (1.0)	1 (0.5)
ウイルス感染	1 (0.5)	0
ウイルス性上気道感染	1 (0.5)	0
臨床検査	4 (1.9)	6 (2.8)
アラニンアミノトランスフェラーゼ増加	1 (0.5)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
臨床検査 (Cont.)		
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.5)	2 (0.9)
血中アルカリホスファターゼ増加	1 (0.5)	0
血中トリグリセリド増加	1 (0.5)	0
ヘモグロビン減少	0	1 (0.5)
肝酵素上昇	0	1 (0.5)
トランスアミナーゼ上昇	1 (0.5)	1 (0.5)
尿潜血陽性	0	1 (0.5)
代謝および栄養障害	2 (1.0)	4 (1.9)
高カリウム血症	1 (0.5)	0
高脂血症	1 (0.5)	1 (0.5)
高尿酸血症	0	2 (0.9)
低コレステロール血症	0	1 (0.5)
筋骨格系および結合組織障害	3 (1.4)	0
関節痛	2 (1.0)	0
軸性脊椎関節炎	1 (0.5)	0
背部痛	1 (0.5)	0
四肢痛	1 (0.5)	0
神経系障害	3 (1.4)	3 (1.4)
味覚消失	0	1 (0.5)
浮動性めまい	1 (0.5)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Placebo (N=209) n (%)	Upadacitinib 15 mg QD (N=211) n (%)
神経系障害 (Cont.)		
頭痛	1 (0.5)	1 (0.5)
感覚鈍麻	1 (0.5)	0
失神	0	1 (0.5)
精神障害	1 (0.5)	0
不安	1 (0.5)	0
腎および尿路障害	0	2 (0.9)
血尿	0	2 (0.9)
呼吸器、胸郭および縦隔障害	2 (1.0)	2 (0.9)
咳嗽	1 (0.5)	0
口腔咽頭痛	1 (0.5)	0
呼吸障害	0	2 (0.9)
皮膚および皮下組織障害	0	3 (1.4)
ざ瘡	0	2 (0.9)
斑状出血	0	1 (0.5)
血管障害	1 (0.5)	0
高血圧	1 (0.5)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days of the treatment after the last dose of study treatment in Double-Blind Period.

Program Source Code: [redacted]
相互参照：M19-944試験 Study 1 中間CSR TABLE 14.3__1.3.4.1

表 3. 長期投与データにおける有害事象；100 人年あたりの発現率（MedDRA SOC 及び PT 別）（M19-944 試験，安全性解析対象集団）

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
Any adverse event	453 (168.6)
血液およびリンパ系障害	39 (14.5)
貧血	5 (1.9)
失血性貧血	1 (0.4)
鉄欠乏性貧血	1 (0.4)
白血球増加症	1 (0.4)
白血球減少症	12 (4.5)
リンパ球増加症	1 (0.4)
リンパ球減少症	3 (1.1)
好中球減少症	15 (5.6)
先天性、家族性および遺伝性障害	1 (0.4)
先天性大動脈弁狭窄	1 (0.4)
耳および迷路障害	1 (0.4)
外耳の炎症	1 (0.4)
内分泌障害	1 (0.4)
甲状腺腫瘤	1 (0.4)
眼障害	7 (2.6)
眼瞼炎	2 (0.7)
遠視	1 (0.4)
虹彩毛様体炎	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
眼障害 (Cont.)	
虹彩炎	1 (0.4)
ぶどう膜炎	2 (0.7)
胃腸障害	53 (19.7)
腹部膨満	2 (0.7)
腹痛	4 (1.5)
上腹部痛	3 (1.1)
裂肛出血	1 (0.4)
口角口唇炎	1 (0.4)
アフタ性潰瘍	6 (2.2)
慢性胃炎	1 (0.4)
便秘	2 (0.7)
クローン病	1 (0.4)
下痢	4 (1.5)
憩室	1 (0.4)
十二指腸炎	1 (0.4)
消化不良	1 (0.4)
食中毒	1 (0.4)
胃炎	2 (0.7)
胃食道逆流性疾患	3 (1.1)
痔出血	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
胃腸障害 (Cont.)	
痔核	1 (0.4)
裂孔ヘルニア	1 (0.4)
口腔内潰瘍形成	2 (0.7)
悪心	7 (2.6)
嚥下痛	1 (0.4)
幽門痙攣	1 (0.4)
歯痛	1 (0.4)
上部消化管出血	1 (0.4)
食道静脈瘤	1 (0.4)
嘔吐	2 (0.7)
一般・全身障害および投与部位の状態	12 (4.5)
疲労	4 (1.5)
歩行障害	1 (0.4)
注射部位疼痛	2 (0.7)
浮腫	1 (0.4)
疼痛	2 (0.7)
発熱	2 (0.7)
肝胆道系障害	8 (3.0)
急性胆管炎	1 (0.4)
胆石症	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
肝胆道系障害 (Cont.)	
肝嚢胞	1 (0.4)
肝腫瘤	1 (0.4)
脂肪肝	2 (0.7)
胆汁うっ滞性黄疸	1 (0.4)
門脈圧亢進症	1 (0.4)
免疫系障害	2 (0.7)
アナフィラキシー反応	1 (0.4)
季節性アレルギー	1 (0.4)
感染症および寄生虫症	140 (52.1)
無症候性ＣＯＶＩＤ－１９	5 (1.9)
細菌性膣症	2 (0.7)
気管支炎	5 (1.9)
ＣＯＶＩＤ－１９	22 (8.2)
ＣＯＶＩＤ－１９肺炎	12 (4.5)
合併症を伴う虫垂炎	1 (0.4)
結膜炎	2 (0.7)
コクサッキーウイルス感染	1 (0.4)
膀胱炎	4 (1.5)
播種性水痘帯状疱疹ウイルス感染	1 (0.4)
耳感染	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
感染症および寄生虫症 (Cont.)	
熱性感染症	2 (0.7)
皮膚真菌感染	2 (0.7)
胃腸炎	4 (1.5)
消化管感染	2 (0.7)
歯肉炎	1 (0.4)
ヘリコバクター性胃炎	1 (0.4)
帯状疱疹	10 (3.7)
麦粒腫	1 (0.4)
潜伏結核	5 (1.9)
上咽頭炎	14 (5.2)
爪真菌症	1 (0.4)
口腔カンジダ症	1 (0.4)
爪囲炎	1 (0.4)
腹膜炎	1 (0.4)
咽頭炎	5 (1.9)
肺炎	1 (0.4)
歯髄炎	2 (0.7)
慢性腎盂腎炎	1 (0.4)
気道感染	1 (0.4)
鼻炎	2 (0.7)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
感染症および寄生虫症 (Cont.)	
副鼻腔炎	6 (2.2)
白癬感染	1 (0.4)
歯膿瘍	1 (0.4)
歯感染	1 (0.4)
上気道感染	10 (3.7)
尿路感染	3 (1.1)
水痘	1 (0.4)
ウイルス性咽頭炎	1 (0.4)
ウイルス性上気道感染	2 (0.7)
傷害、中毒および処置合併症	22 (8.2)
動物咬傷	1 (0.4)
脳振盪	1 (0.4)
挫傷	3 (1.1)
転倒	3 (1.1)
靭帯断裂	1 (0.4)
半月板損傷	1 (0.4)
多発性外傷	1 (0.4)
筋損傷	1 (0.4)
肉離れ	1 (0.4)
交通事故	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
傷害、中毒および処置合併症 (Cont.)	
皮膚擦過傷	1 (0.4)
皮膚裂傷	2 (0.7)
軟部組織損傷	1 (0.4)
ストレス骨折	1 (0.4)
外傷性骨折	1 (0.4)
有毒性刺傷	1 (0.4)
創傷	1 (0.4)
臨床検査	44 (16.4)
アラニンアミノトランスフェラーゼ増加	9 (3.3)
アスパラギン酸アミノトランスフェラーゼ増加	10 (3.7)
血中重炭酸塩減少	1 (0.4)
血中ビリルビン増加	1 (0.4)
血中ブドウ糖増加	1 (0.4)
血圧異常	1 (0.4)
血中トリグリセリド増加	2 (0.7)
尿中血陽性	2 (0.7)
ヘモグロビン減少	2 (0.7)
心拍数減少	1 (0.4)
肝酵素上昇	1 (0.4)
リンパ球形態異常	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
臨床検査 (Cont.)	
好中球数減少	1 (0.4)
血小板数増加	1 (0.4)
尿中蛋白陽性	1 (0.4)
血沈亢進	1 (0.4)
トランスアミナーゼ上昇	2 (0.7)
尿潜血陽性	2 (0.7)
体重増加	1 (0.4)
白血球数減少	3 (1.1)
代謝および栄養障害	30 (11.2)
糖尿病	1 (0.4)
脂質異常症	2 (0.7)
耐糖能障害	1 (0.4)
高コレステロール血症	4 (1.5)
高血糖	4 (1.5)
高カリウム血症	1 (0.4)
高脂血症	3 (1.1)
高トリグリセリド血症	3 (1.1)
高尿酸血症	7 (2.6)
低コレステロール血症	1 (0.4)
低カリウム血症	2 (0.7)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
代謝および栄養障害 (Cont.)	
代謝性アシドーシス	1 (0.4)
筋骨格系および結合組織障害	14 (5.2)
関節炎	1 (0.4)
背部痛	6 (2.2)
筋痙縮	1 (0.4)
筋緊張	1 (0.4)
筋骨格系胸痛	1 (0.4)
頚部痛	1 (0.4)
変形性関節症	1 (0.4)
滑膜炎	1 (0.4)
腱炎	1 (0.4)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	4 (1.5)
基底細胞癌	1 (0.4)
リンパ増殖性障害	1 (0.4)
子宮平滑筋腫	2 (0.7)
神経系障害	19 (7.1)
味覚消失	1 (0.4)
手根管症候群	1 (0.4)
浮動性めまい	1 (0.4)
頭痛	12 (4.5)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
神経系障害 (Cont.)	
片頭痛	1 (0.4)
神経圧迫	1 (0.4)
失神	1 (0.4)
振戦	1 (0.4)
精神障害	3 (1.1)
不安	1 (0.4)
易刺激性	1 (0.4)
リビドー亢進	1 (0.4)
腎および尿路障害	12 (4.5)
尿路結石	3 (1.1)
血尿	3 (1.1)
水腎症	1 (0.4)
腎結石症	1 (0.4)
腎仙痛	1 (0.4)
腎嚢胞	1 (0.4)
尿管結石症	2 (0.7)
生殖系および乳房障害	5 (1.9)
乳房腫瘤	1 (0.4)
骨盤痛	1 (0.4)
前立腺炎	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
生殖系および乳房障害 (Cont.)	
腟嚢胞	2 (0.7)
呼吸器、胸郭および縦隔障害	11 (4.1)
急性呼吸不全	1 (0.4)
アレルギー性咳嗽	1 (0.4)
咳嗽	2 (0.7)
呼吸困難	1 (0.4)
鼻出血	1 (0.4)
口腔咽頭痛	2 (0.7)
肺塞栓症	1 (0.4)
呼吸障害	2 (0.7)
皮膚および皮下組織障害	19 (7.1)
ざ瘡	3 (1.1)
脱毛症	1 (0.4)
皮膚炎	1 (0.4)
アレルギー性皮膚炎	1 (0.4)
アトピー性皮膚炎	1 (0.4)
接触皮膚炎	1 (0.4)
びまん性脱毛症	1 (0.4)
斑状出血	3 (1.1)
爪破損	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
皮膚および皮下組織障害 (Cont.)	
そう痒症	1 (0.4)
乾癬	1 (0.4)
発疹	1 (0.4)
紅斑性皮疹	1 (0.4)
脂漏性皮膚炎	1 (0.4)
皮膚刺激	1 (0.4)
血管障害	6 (2.2)
高血圧	5 (1.9)
静脈瘤	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]
相互参照：M19-944試験 Study 1 中間CSR TABLE 14.3__1.2.1.2

表 4. 長期投与データにおける治験薬と関連ありの有害事象；100 人年あたりの発現率（MedDRA SOC 及び PT 別）（M19-944 試験，安全性解析対象集団）

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
Any adverse event	155 (57.7)
血液およびリンパ系障害	35 (13.0)
貧血	3 (1.1)
白血球増加症	1 (0.4)
白血球減少症	12 (4.5)
リンパ球増加症	1 (0.4)
リンパ球減少症	3 (1.1)
好中球減少症	15 (5.6)
眼障害	3 (1.1)
眼瞼炎	2 (0.7)
ぶどう膜炎	1 (0.4)
胃腸障害	16 (6.0)
腹部膨満	1 (0.4)
腹痛	2 (0.7)
上腹部痛	1 (0.4)
アフタ性潰瘍	3 (1.1)
慢性胃炎	1 (0.4)
便秘	1 (0.4)
下痢	2 (0.7)
胃食道逆流性疾患	2 (0.7)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
胃腸障害 (Cont.)	
悪心	2 (0.7)
嘔吐	1 (0.4)
一般・全身障害および投与部位の状態	2 (0.7)
疲労	1 (0.4)
浮腫	1 (0.4)
感染症および寄生虫症	45 (16.7)
無症候性ＣＯＶＩＤ－１９	1 (0.4)
細菌性膣症	2 (0.7)
気管支炎	2 (0.7)
ＣＯＶＩＤ－１９	3 (1.1)
ＣＯＶＩＤ－１９肺炎	1 (0.4)
膀胱炎	3 (1.1)
播種性水痘帯状疱疹ウイルス感染	1 (0.4)
熱性感染症	2 (0.7)
皮膚真菌感染	1 (0.4)
胃腸炎	1 (0.4)
消化管感染	1 (0.4)
帯状疱疹	10 (3.7)
潜伏結核	2 (0.7)
上咽頭炎	3 (1.1)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
感染症および寄生虫症 (Cont.)	
肺炎	1 (0.4)
歯髄炎	1 (0.4)
副鼻腔炎	3 (1.1)
歯感染	1 (0.4)
上気道感染	5 (1.9)
尿路感染	1 (0.4)
臨床検査	21 (7.8)
アラニンアミノトランスフェラーゼ増加	4 (1.5)
アスパラギン酸アミノトランスフェラーゼ増加	8 (3.0)
血中重炭酸塩減少	1 (0.4)
尿中血陽性	1 (0.4)
ヘモグロビン減少	1 (0.4)
肝酵素上昇	1 (0.4)
トランスアミナーゼ上昇	2 (0.7)
尿潜血陽性	1 (0.4)
白血球数減少	2 (0.7)
代謝および栄養障害	13 (4.8)
高コレステロール血症	2 (0.7)
高血糖	1 (0.4)
高カリウム血症	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
代謝および栄養障害 (Cont.)	
高脂血症	2 (0.7)
高トリグリセリド血症	2 (0.7)
高尿酸血症	2 (0.7)
低コレステロール血症	1 (0.4)
低カリウム血症	1 (0.4)
代謝性アシドーシス	1 (0.4)
筋骨格系および結合組織障害	1 (0.4)
筋骨格系胸痛	1 (0.4)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (1.1)
リンパ増殖性障害	1 (0.4)
子宮平滑筋腫	2 (0.7)
神経系障害	3 (1.1)
味覚消失	1 (0.4)
頭痛	1 (0.4)
失神	1 (0.4)
精神障害	1 (0.4)
不安	1 (0.4)
腎および尿路障害	2 (0.7)
血尿	2 (0.7)
生殖系および乳房障害	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 24.0 System Organ Class Preferred Term	Any Upadacitinib 15 mg QD (N=414) (PYs=268.7) Events (E/100PYs)
生殖系および乳房障害 (Cont.)	
腟嚢胞	1 (0.4)
呼吸器、胸郭および縦隔障害	3 (1.1)
肺塞栓症	1 (0.4)
呼吸障害	2 (0.7)
皮膚および皮下組織障害	6 (2.2)
ざ瘡	3 (1.1)
皮膚炎	1 (0.4)
アトピー性皮膚炎	1 (0.4)
斑状出血	1 (0.4)

Note: Treatment-emergent Adverse Event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of study treatment, and no more than 30 days after the last dose of study treatment in the study.
E/100PYs = Events per 100 patient-years.

Program Source Code: [redacted]
相互参照：M19-944試験 Study 1 中間CSR TABLE 14.3__1.3.4.2

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血				X
アスパラギン酸アミノトランスフェラーゼ増加				X
失血性貧血	X			X
肝嚢胞				X
肝腫瘤				X
門脈圧亢進症				X
上部消化管出血	X			
食道静脈瘤	X	X		X

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 15 MG QD /P2:ABT-494 15 MG QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
MEDICAL HISTORY: RIGHT KNEE PAIN	19[redacted]
MEDICAL HISTORY: SEASONAL ALLERGIES	19[redacted]
MEDICAL HISTORY: RIGHT ELBOW PAIN	19[redacted]
MEDICAL HISTORY: DIABETES	19[redacted]
MEDICAL HISTORY: COPD CHRONIC OBSTRUCTIVE PULMONARY DISEASE.	20[redacted]
MEDICAL HISTORY: FATTY LIVER	20[redacted]
MEDICAL HISTORY: ACID REFLUX	20[redacted]
MEDICAL HISTORY: HISTORY OF KIDNEY STONES	20[redacted]
AXIAL SPONDYLOARTHRITIS DISEASE HISTORY: AXIAL SPONDYLOARTHRITIS	20[redacted]
MEDICAL HISTORY: BACK PAIN	20[redacted]
MEDICAL HISTORY: CATARACT LEFT EYE	20[redacted]
MEDICAL HISTORY: CATARACT RIGHT EYE	20[redacted]
MEDICAL HISTORY: CORONARY ARTERY DISEASE	20[redacted]
MEDICAL HISTORY: HYPERTENSION	20[redacted]
MEDICAL HISTORY: ANEMIA	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: SURGERY RIGHT KNEE	19[redacted]
PRIOR PROCEDURES: INJURED RIGHT ELBOW	19[redacted]
PRIOR PROCEDURES: BACK SURGERY	20[redacted]
PRIOR PROCEDURES: SPINAL STIMULATOR INSERTION	20[redacted]
PRIOR PROCEDURES: SPINAL STIMULATOR REMOVED	20[redacted]
PRIOR PROCEDURES: LASER SURGERY	20[redacted]
PRIOR PROCEDURES: LASER SURGERY LEFT EYE.	20[redacted]
PRIOR PROCEDURES: CARDIAC STENTS	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	15 CIGARETTE	10	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 mg	ORAL	QD	[redacted] / 1	[redacted] / 100	100
ABT-494	15 mg	ORAL	QD	[redacted] / 101	[redacted] / 392	292

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CELECOXIB	200 mg	BID	Y-M: 20[redacted]
MELOXICAM	15 mg	QD	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	NOT REPORTED	QD	Y-M: 20[redacted]
ATENOLOL	50 mg	QD	Y-M: 20[redacted]
GLIPIZIDE	10 mg	BID	Y-M: 20[redacted]
METFORMIN	1000 mg	BID	Y-M: 20[redacted]
METOCLOPRAMIDE	10 mg	TID	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]

SECUKINUMAB	150 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
CODEINE PHOSPHATE;PARACETAMOL	30 mg	BID	Y-M: 20[redacted]
CYANOCOBALAMIN	1000 mg	OTHER: MONTHLY	Y-M: 20[redacted] / -69

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
METFORMIN	1000 MG	BID	Y-M: 20[redacted]	ONGOING
METOCLOPRAMIDE	10 MG	TID	Y-M: 20[redacted]	ONGOING
ATENOLOL	50 MG	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 162
GLIPIZIDE	10 MG	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 201
ACETYLSALICYLIC ACID	NOT REPORTED	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 396
OMEPRAZOLE	20 MG	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 396
CODEINE PHOSPHATE;PARACETAMOL	30 MG	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 399
CYANOCOBALAMIN	1000 MG	OTHER: MONTHLY	Y-M: 20[redacted] / -69	Y-M: 20[redacted] / 201
ATENOLOL	25 MG	QD	Y-M: 20[redacted] / 162	ONGOING
BLOOD, WHOLE	1 OTHER: UNIT OF PRBC	OTHER: ONCE	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 393
OMEPRAZOLE	20 MG	BID	Y-M: 20[redacted] / 396	ONGOING
PROPRANOLOL	20 MG	TID	Y-M: 20[redacted] / 396	ONGOING
SUCRALFATE	1 OTHER: GRAM	QID	Y-M: 20[redacted] / 396	ONGOING

Event #1: Event of Interest - Drug Related Hepatic Disorders

Event Description	ELEVATED AST
Preferred Term	アスパラギン酸アミノトランスフェラーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 171
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	212
Duration of AE	42 DAYS

Severity	Grade 1
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event, Event of Interest - Non-hemolytic and Non-aplastic Anemias

Event Description	ACUTE BLOOD LOSS ANEMIA
Preferred Term	失血性貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 392
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 392): ELECTRICARDIOGRAM:RIGHT BUNDLE BRANCH BLOCK.; [redacted]20[redacted] (RX DAY 393): BLOOD TRANSFUSION:INCREASE IN HEMOGLOBIN AND HEMATOCRIT LEVELS.; [redacted]20[redacted] (RX DAY 395): BANDING OF ESOPHAGEAL VARICIES:ESOPHAGEAL VARICIES WERE BANDED TO PREVENT FUTURE BLEEDING.; CHEST XRAY:NO ACUTE CARDIOPULMONARY DISEASE.; CT OF ABDOMEN AND PELVIS WITH AND WITHOUT CONTRAST:SHRUNKEN AND NODULAR LIVER, SCATTERED DIVERTICULOSIS , RIGHT RENAL CORTICAL CYSTS AND SCATTERED ATHEROSCLEROTIC CALCIFICATION OF THE INFRARENAL AORTA AND BILATERAL COMMON ILIAC ARTERIES; ESOPHGOGASTRODUODENOSCOPY:ESOPHAGEAL VARICES GASTROESPPHAGEAL REFLUX DISEASE, HYPERTENSIVE GASTROPATHY, HIATAL HERNIA.

AE Stopped Rx Day	396 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	Grade 3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THE PI STATES THE FATTY LIVER LED TO CIRRHOSIS AND THEN TO THE SAE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING

Event #3: Event of Interest - Drug Related Hepatic Disorders

Event Description	CYST ON LIVER
Preferred Term	肝嚢胞

AE Onset Date / Rx Day	[redacted]20[redacted] / 392
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	Grade 1
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Event of Interest - Drug Related Hepatic Disorders

Event Description	SHRUNKEN AND NODULAR LIVER
Preferred Term	肝腫瘤
AE Onset Date / Rx Day	[redacted]20[redacted] / 392
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	Grade 1
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #5: Serious Adverse Event

Event Description	UPPER GASTROINTESTIONAL HEMORRHAGE
Preferred Term	上部消化管出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 392
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	395 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	Grade 3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ESOPHAGEAL VARICIES.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING

Event #6: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Drug Related Hepatic Disorders

Event Description	ESOPHAGEAL VARICES
Preferred Term	食道静脈瘤
AE Onset Date / Rx Day	[redacted]20[redacted] / 392
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 392): ALBUMIN: 30 [34 - 50] G/L; ALBUMIN: 30 [34 - 50] G/L; ALKALINE PHOSPHATASE: 93 [46 - 116] U/L; BILIRUBIN: 24 [3 - 17] UMOL/L; BLOOD UREA NITROGEN: 9.6 [2.5 - 6.4] MMOL/L; CALCIUM: 1.92 [2.12 - 2.52] MMOL/L; CHLORIDE: 112 [98 - 107] MMOL/L; CREATININE: 79 [53 - 106] UMOL/L; EOSINOPHILS: 0.02 [0.04 - 0.54] 10^9/L; EOSINOPHILS/LEUKOCYTES: 0.3 [0.8 - 7] %; ERYTHROCYTES: 3 [4.6 - 6.1] 10^12/L; GLUCOSE: 9 [3.9 - 5.5] MMOL/L; HEMATOCRIT: 0.29 [0.4 - 0.49] FRACTION OF 1; HEMOGLOBIN: 93 [131 - 160] G/L; LEUKOCYTES: 7.1 [4.2 - 9.1] 10^9/L; LYMPHOCYTES: 1.01 [1.32 - 3.57] 10^9/L; LYMPHOCYTES/LEUKOCYTES: 14.2 [21.8 - 53.1] %; NPTST002-ABS IMMAT GRAN (AUTO): 0.0500 [0 - NOT REPORTED] 10^3/UL; NPTST006-AST: 33 [15 - 37] U/L; NPTST014-BUN/CREATININE RATIO: 30.3 [6 - 20] RATIO; NPTST017-CARBON DIOXIDE: 25 [22 - 29] MEQ/L; NPTST020-CK-MB (CK-2): 2.1 [0 - 3.6] NG/ML; NPTST034-IMM/TOT GRANULO (AUTO): 0.7 [0 - 0.43] %; NPTST041-LIPASE: 50 [73 - 393] U/L; NPTST042-MAGNESIUM: 1.7 [1.8 - 2.4] MG/DL; NPTST044-MCHC: 31.6 [32.3 - 36.5] G/DL; NPTST045-MCV: 96.7 [79 - 92.2] FL; NPTST065-PT: 13.3 [9.2 - 11.7] SECONDS; NPTST070-RDW COEFF OF VAR: 16.2 [11.6 - 14.4] %; NPTST071-RDW STD DEVIATION: 57.3 [35.1 - 43.9] FL; NPTST080-TOTAL CREATINE KINASE: 181 [39 - 308] U/L; NPTST083-

TROPONIN I: 0.02 [0 - 0.05] NG/ML; NPTST084-UR SPECIFIC GRAVITY: 1.03 [1.02 - 1.02] SEC; NPTST087-URINE PH: 5 [5 - 7] SECONDS; NEUTROPHILS: 5.43 [1.78 - 5.38] 10^9/L; NEUTROPHILS/LEUKOCYTES: 76.5 [34 - 67.9] %; PLATELETS: 152 [163 - 337] 10^9/L; POTASSIUM: 3.6 [3.6 - 5.2] MMOL/L; PROTEIN: 58 [64 - 82] G/L; PROTHROMBIN INTL. NORMALIZED RATIO: 1.26 [0.88 - 1.12] RATIO; SODIUM: 144 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 393): ALBUMIN: 23 [34 - 50] G/L; BLOOD UREA NITROGEN: 8.6 [2.5 - 7.1] MMOL/L; CHLORIDE: 113 [96 - 106] MMOL/L; CREATININE: 65 [53 - 106] UMOL/L; ERYTHROCYTES: 2.4 [4.6 - 6.1] 10^12/L; GLUCOSE: 11 [3.9 - 5.5] MMOL/L; HEMATOCRIT: 0.24 [0.4 - 0.49] FRACTION OF 1; HEMOGLOBIN: 75 [131 - 160] G/L; LEUKOCYTES: 5.5 [4.2 - 9.1] 10^9/L; LYMPHOCYTES: 1.21 [1.32 - 3.57] 10^9/L; NPTST017-CARBON DIOXIDE: 26 [21 - 32] MMOL/L; NPTST044-MCHC: 31.9 [32.3 - 36.5] G/DL; NPTST045-MCV: 96.7 [79 - 92.2] FL; NPTST070-RDW COEFF OF VAR: 16.2 [11.6 - 14.4] %; NPTST071-RDW STD DEVIATION: 57.6 [35.1 - 43.9] FL; PLATELETS: 110 [163 - 337] 10^9/L; POTASSIUM: 3.6 [3.5 - 5.1] MMOL/L; SODIUM: 142 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 396): ALBUMIN: 30 [34 - 50] G/L; BASOPHILS: 0.02 [0 - 3] 10^9/L; BASOPHILS/LEUKOCYTES: 0.3 [0.2 - 1.2] %; BLOOD UREA NITROGEN: 3.6 [2.5 - 6.4] MMOL/L; CALCIUM: 2 [2.12 - 2.52] MMOL/L; CALCIUM: 2 [2.12 - 2.52] MMOL/L; CHLORIDE: 109 [96 - 106] MMOL/L; CREATININE: 80 [53 - 106] UMOL/L; EOSINOPHILS: 0.11 [0.04 - 0.54] 10^9/L; EOSINOPHILS/LEUKOCYTES: 1.7 [0.8 - 7] %; ERYTHROCYTES: 3 [4.6 - 6.1] 10^12/L; GLUCOSE: 9 [3.9 - 5.5] MMOL/L; HEMATOCRIT: 0.29 [0.4 - 0.49] FRACTION OF 1; HEMOGLOBIN: 93 [131 - 160] G/L; LEUKOCYTES: 6.6 [4.2 - 9.1] 10^9/L; LYMPHOCYTES: 0.45 [1.32 - 3.57] 10^9/L; LYMPHOCYTES/LEUKOCYTES: 6.8 [21.8 - 53.1] %; MONOCYTES: 0.64 [1000 - 4800] 10^9/L; MONOCYTES/LEUKOCYTES: 9.7 [2 - 8] %; NPTST002-ABS IMMAT GRAN (AUTO): 0.07 [0 - 0.03] 10^3/UL; NPTST004-ANION GAP: 6 [5 - 15] MMOL/L; NPTST014-BUN/CREATININE RATIO: 11 [6 - 20] RATIO; NPTST017-CARBON DIOXIDE: 25 [22 - 29] MEQ/L; NPTST034-IMM/TOT GRANULO (AUTO): 1.1 [0 - 0.43] %; NPTST037-IRON: 29 [38.3 - 48.6] %; NPTST043-MCH: 30.8 [27 - 31] PG; NPTST044-MCHC: 31.6 [32.3 - 36.5] G/DL; NPTST045-MCV: 97.4 [79 - 92.2] FL; NPTST052-MPV: 10.9 [9.4 - 12.4] FL; NPTST054-NUCLEATED RBC % (AUTO): 0 [0 - 100] ABSOLUTE COUNT; NPTST055-NUCLEATED RBS'S: 0 [0 - 100] ABSOLUTE COUNT; NPTST060-PHOSPHORUS: 2.6 [2.6 - 4.7] MG/DL; NPTST063-PREALBUMIN: 8.9 [5 - 10.9] DL; NPTST070-RDW COEFF OF VAR: 17.2 [11.6 - 14.4] %; NPTST071-RDW STD DEVIATION: 58.8 [35.1 - 43.9] FL; NPTST079-TIBC: 349 [250 - 450] MCG/DL; NEUTROPHILS: 5.29 [1.78 - 5.38] 10^9/L; NEUTROPHILS/LEUKOCYTES: 80.4 [34 - 67.9] %; PLATELETS: 108 [163 - 337] 10^9/L; POTASSIUM: 3.5 [3.6 - 5.2] MMOL/L; SODIUM: 140 [135 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 392): CHEST X RAY:NORMAL APPEARANCE OF HEART, MEDIASTINUM, AND HILAR AREAS. THE LUNGS ARE CLEAR AND SHOWED NO INFILTRATED. NO PLEURAL ABNORMALITY. NO ACUTE CARDIOPULMONARY DISEASE.; CT ABDOMEN:SHRUNKEN AND NODULAR LIVER A 3.6 X 2.8 CM CYST RIGHT KIDNEY, SCATTERED DIVERTICULOSIS OF THE DISTAL TRANSVERSE,DESCENDING AND SIGMOID COLON WITHOUT DIVERTICULIIS AND SCATERED ATHEROSCLEROTIC CALCIFIC; [redacted]20[redacted] (RX DAY 393): BLOOD TRANSFUSION:TRANSFUSED ONE UNIT OF PACKED RED BLOOD CELLS; [redacted]20[redacted] (RX DAY 395): EGD WITH BANDING:BANDING OF ESOPHAGEAL VARICES; EGD WITH BIOPSY:NO HELICOBACTER PYLORI LIKE ORGANISMS IDENTIFIED. ESOPHAGEAL VARICIES

AE Stopped Rx Day	395 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	Grade 3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CAUSED FROM LIVER CIRRHOSIS
Discontinued Study Drug Due to the Event	YES

SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING

Event #7: Event of Interest - Drug Related Hepatic Disorders

Event Description	PORTAL HYPERTENSION
Preferred Term	門脈圧亢進症
AE Onset Date / Rx Day	[redacted]20[redacted] / 395 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Grade 2
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #8: Event of Interest - Non-hemolytic and Non-aplastic Anemias

Event Description	ANEMIA
Preferred Term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 420 (28 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Grade 2
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY

Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted] 20[redacted]:14:15

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M19-944

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性で，米国アッヴィ社の ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及びウパダシチニブが投与され，急性失血性貧血，食道静脈瘤及び上部消化管出血を発現した。

Event 2，5 及び 6 の臨床経過：

関連病歴は，糖尿病，慢性閉塞性肺疾患，脂肪肝，酸逆流，冠動脈疾患，高血圧，軸性脊椎関節炎，貧血，元喫煙者（1 日 15 本を 10 年間）及び非飲酒者であった。

被験者は 14 週時までは盲検化プラセボ対照期に参加していた。投与開始から 101 日後，被験者はウパダシチニブの非盲検投与期に移行した。

投与開始から 392 日後，被験者は急性失血性貧血，食道静脈瘤及び上部消化管出血を発現した。投与開始から 395 日後，食道静脈瘤及び上部消化管出血は消失した。投与開始から 396 日後，急性失血性貧血は消失した。

投与開始から 392 日後，被験者は腹痛，悪心及び吐血のため入院した。投与開始から 395 日後，被験者は上部消化管内視鏡検査を受け，食道静脈瘤が認められたためバンドで結紮された。投与開始から 396 日後，被験者は退院した。

被験者は輸血を受けた。

The patient's past medications include:

CELEBREX for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MOBIC for AXIAL SPONDYLOARTHRITIS [redacted] 20[redacted] - [redacted] 20[redacted])

COSENTYX for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute blood loss anemia (10082299) (Blood loss anaemia (10082297)) [v.24.0] [10082299]

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

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

Dechallenge: Not Applicable

2) Esophageal varices (10015452) (Varices oesophageal (10056091)) [v.24.0] [10015452]

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

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

Dechallenge: Not Applicable

3) Upper gastrointestinal hemorrhage (10055356) (Upper gastrointestinal haemorrhage (10046274)) [v.24.0] [10055356]

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

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

Dechallenge: Not Applicable

Causality for UPADACITINIB (Open Label)

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1) Acute blood loss anemia (10082299) (Blood loss anaemia (10082297)) [v.24.0] [10082299]

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

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

Dechallenge: Not Applicable

2) Esophageal varices (10015452) (Varices oesophageal (10056091)) [v.24.0] [10015452]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

3) Upper gastrointestinal hemorrhage (10055356) (Upper gastrointestinal haemorrhage (10046274)) [v.24.0] [10055356]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE BLOOD LOSS ANEMIA

- **Investigator:** Not applicable

- **AbbVie:** Event more likely related to concurrent upper gastrointestinal hemorrhage and esophageal varices.

Event of ESOPHAGEAL VARICES

- **Investigator:** Not Applicable

- **AbbVie:** Event is more likely related to pre-existing fatty liver since 20[redacted] with concurrent shrunken and nodular liver (per CT abdomen) and hypertensive gastropathy (per EGD)

Event of UPPER GASTROINTESTINAL HEMORRHAGE

- **Investigator:** Esophageal varices

- **AbbVie:** Event more likely related to the concurrent event of esophageal varices with shrunken and nodular liver (per CT abdomen), hypertensive gastropathy (per EGD) and pre-existing fatty liver since 20[redacted].

Alternative Etiology for UPADACITINIB (Open Label)

Event of ACUTE BLOOD LOSS ANEMIA

- **Investigator:** Not applicable

- **AbbVie:** Event more likely related to concurrent upper gastrointestinal hemorrhage and esophageal varices.

Event of ESOPHAGEAL VARICES

- **Investigator:** Not Applicable

- **AbbVie:** Event is more likely related to pre-existing fatty liver since 20[redacted] with concurrent shrunken and nodular liver (per CT abdomen) and hypertensive gastropathy (per EGD)

Event of UPPER GASTROINTESTINAL HEMORRHAGE

- **Investigator:** Esophageal varices

- **AbbVie:** Event more likely related to the concurrent event of esophageal varices with shrunken and nodular liver (per CT abdomen), hypertensive gastropathy (per EGD) and pre-existing fatty liver since 20[redacted].

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **CHEST X-RAY:** NO ACUTE CARDIOPULMONARY DISEASE.

[redacted] 20[redacted] **CHEST XRAY:** NORMAL APPEARANCE OF HEART, MEDIASTINUM, AND HILAR AREAS. THE LUNGS ARE CLEAR AND SHOWED NO INFILTRATED. NO PLEURAL ABNORMALITY. NO ACUTE CARDIOPULMONARY DISEASE.

[redacted] 20[redacted] **CT ABDOMEN AND PELVIS:** SHRUNKEN AND NODULAR LIVER, SCATTERED DIVERTICULOSIS , RIGHT RENAL CORTICAL CYSTS AND SCATTERED ATHEROSCLEROTIC CALCIFICATION OF THE INFRARENAL AORTA AND BILATERAL COMMON ILIAC ARTERIES

[redacted] 20[redacted] **EGD:** NO HELICOBACTER PYLORI LIKE ORGANISMS IDENTIFIED. ESOPHAGEAL VARICIES GASTROESPPHAGEAL REFLUX DISEASE, HYPERTENSIVE GASTROPATHY, HIATAL HERNIA.

[redacted] 20[redacted] **EKG:** RIGHT BUNDLE BRANCH BLOCK.

[redacted] 20[redacted] **HEMATOCRIT:** 29.4% (normal 39.6 to 48.7)

[redacted] 20[redacted] **HEMATOCRIT:** 23.5% (normal 39.6 to 48.7)

[redacted] 20[redacted] **HEMATOCRIT:** 29.4% (normal 39.6 to 48.7)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.3 G/DL (normal 13.1 to 16.0)

[redacted] 20[redacted] **HEMOGLOBIN:** 7.5 G/DL (normal 13.1 to 16.0)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.3 G/DL (normal 13.1 to 16.0)

[redacted] 20[redacted] **INR:** 1.26 ratio (normal 0.88 to 1.12)

[redacted] 20[redacted] **IRON:** 29% (normal 38.3 to 48.6)

[redacted] 20[redacted] **LIPASE:** 50 U/L (normal 73 to 393)

20[redacted] **LIVER BIOPSY:** Not reported

[redacted] 20[redacted] **PLATELET COUNT:** 152 X10**3/MCL (normal 163 to 337)

[redacted] 20[redacted] **PLATELET COUNT:** 108 X10**3/MCL (normal 163 to 337)

[redacted] 20[redacted] **PT:** 13.3 SEC (normal 9.2 to 11.7)

[redacted] 20[redacted] **SCREENING HEP B SURFACE AGII:** Negative

[redacted] 20[redacted] **SCREENING HEPATITIS C VIRUS ANTIBODY:** Negative

[redacted] 20[redacted] **TOTAL IRON BINDING CAPACITY:** 349 MCG/DL (normal 250 to 450)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Anaemia: Other action taken, subject instructed to stop taking all aspirin or aspirin containing products and all NSAIDS.

被験者番号 [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	X		X

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 15 MG QD /P2:ABT-494 15 MG QD	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
MEDICAL HISTORY: HIATAL HERNIA	19[redacted]
MEDICAL HISTORY: CHRONIC FATIGUE	20[redacted]
MEDICAL HISTORY: IRRITABLE BOWEL SYNDROME	20[redacted]
MEDICAL HISTORY: GALL STONES	20[redacted]
AXIAL SPONDYLOARTHRITIS DISEASE HISTORY: AXIAL SPONDYLOARTHRITIS	20[redacted]
MEDICAL HISTORY: MORPHINE ALLERGY	20[redacted]
MEDICAL HISTORY: NEUROCARDIOGENIC SYNCOPE	20[redacted]
MEDICAL HISTORY: MIGRAINES	20[redacted]
MEDICAL HISTORY: HYPOTHYROID	20[redacted]
MEDICAL HISTORY: ADRENAL INSUFFICIENCY	20[redacted]
MEDICAL HISTORY: ADHD	20[redacted]
MEDICAL HISTORY: ANXIETY	20[redacted]
MEDICAL HISTORY: GEODON ALLERGY	20[redacted]
MEDICAL HISTORY: DILAUDID ALLERGY	20[redacted]
MEDICAL HISTORY: INTERSTITIAL CYSTITIS	20[redacted]
MEDICAL HISTORY: SEASONAL ALLERGIES	20[redacted]
MEDICAL HISTORY: DRY MOUTH	20[redacted]
MEDICAL HISTORY: TACHYCARDIA	20[redacted]
MEDICAL HISTORY: VITAMIN D DEFICIENCY	20[redacted]
MEDICAL HISTORY: VYVANSE ALLERGY	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: FUNDOPLICATION	19[redacted]
PRIOR PROCEDURES: CHOLECYSTECTOMY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 98	98
ABT-494	15 mg	ORAL	QD	[redacted]20[redacted] / 99	[redacted]20[redacted] / 102	4

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
NAPROXEN	500 mg	BID	Y-M: 20[redacted]
LEVOTHYROXINE SODIUM	50 ug	QD	Y-M: 20[redacted]
ONDANSETRON	8 mg	OTHER: PRN TID	Y-M: 20[redacted]
METHOCARBAMOL	750 mg	OTHER: PRN TID	Y-M: 20[redacted]
ETANERCEPT	50 mg	OTHER: Q WEEK	Y-M: 20[redacted]
MILNACIPRAN HYDROCHLORIDE	75 mg	BID	Y-M: 20[redacted]
CELECOXIB	200 mg	BID	Y-M: 20[redacted]
GABAPENTIN	600 mg	OTHER: 6 TIMES PER DAY	Y-M: 20[redacted]
DICLOFENAC	NOT REPORTED	BID	Y-M: 20[redacted]
ARMODAFINIL	250 mg	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
LURASIDONE HYDROCHLORIDE	60 mg	QD	Y-M: 20[redacted]
MECLOZINE	25 mg	OTHER: PRN BID	Y-M: 20[redacted]

VORTIOXETINE HYDROBROMIDE	20 mg	QD	Y-M: 20[redacted]
MONTELUKAST SODIUM	10 mg	QD	Y-M: 20[redacted]
PILOCARPINE HYDROCHLORIDE	5 mg	BID	Y-M: 20[redacted]
METOPROLOL TARTRATE	50 mg	OTHER: HS	Y-M: 20[redacted]
COLECALCIFEROL	50000 IU	OTHER: Q WEEK	Y-M: 20[redacted]
ETHINYLESTRADIOL;LEVONORGESTREL	.15 MG / 30 MCG mg	QD	Y-M: 20[redacted] / -361
BUPRENORPHINE HYDROCHLORIDE	450 ug	QD	Y-M: 20[redacted] / -300

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
LEVOTHYROXINE SODIUM	50 UG	QD	Y-M: 20[redacted]	NOT REPORTED
ONDANSETRON	8 MG	OTHER: PRN TID	Y-M: 20[redacted]	NOT REPORTED
METHOCARBAMOL	750 MG	OTHER: PRN TID	Y-M: 20[redacted]	NOT REPORTED
MILNACIPRAN HYDROCHLORIDE	75 MG	BID	Y-M: 20[redacted]	NOT REPORTED
GABAPENTIN	600 MG	OTHER: 6 TIMES PER DAY	Y-M: 20[redacted]	NOT REPORTED
DICLOFENAC	NOT REPORTED	BID	Y-M: 20[redacted]	NOT REPORTED
ARMODAFINIL	250 MG	QD	Y-M: 20[redacted]	NOT REPORTED
PREDNISONE	5 MG	QD	Y-M: 20[redacted]	NOT REPORTED
LURASIDONE HYDROCHLORIDE	60 MG	QD	Y-M: 20[redacted]	NOT REPORTED
MECLOZINE	25 MG	OTHER: PRN BID	Y-M: 20[redacted]	NOT REPORTED
VORTIOXETINE HYDROBROMIDE	20 MG	QD	Y-M: 20[redacted]	NOT REPORTED
MONTELUKAST SODIUM	10 MG	QD	Y-M: 20[redacted]	NOT REPORTED
PILOCARPINE HYDROCHLORIDE	5 MG	BID	Y-M: 20[redacted]	NOT REPORTED
METOPROLOL TARTRATE	50 MG	OTHER: HS	Y-M: 20[redacted]	NOT REPORTED
COLECALCIFEROL	50000 IU	OTHER: Q WEEK	Y-M: 20[redacted]	NOT REPORTED
ETHINYLESTRADIOL;LEVONORGESTREL	.15 MG / 30 MCG MG	QD	Y-M: 20[redacted] / -361	Y-M: 20[redacted] / 103
INFLIXIMAB	500 MG	OTHER: LOADING DOSE; WEEK 0, WEEK 2, WEEK 6	Y-M: 20[redacted] / 140	Y-M: 20[redacted] / 188
INFLIXIMAB	500 MG	OTHER: Q 6 WEEKS	Y-M: 20[redacted] / 231	NOT REPORTED

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Cardiovascular Events, Event of Interest - Adjudicated Thrombotic Events

Event Description	PULMONARY EMBOLISM
Preferred Term	肺塞栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 103 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 103): ALANINE AMINOTRANSFERASE: 15 [NOT REPORTED - 35] U/L; ALKALINE PHOSPHATASE: 40 [38 - 126] U/L; ASPARTATE AMINOTRANSFERASE: 27 [14 - 36] U/L; BILIRUBIN: 2 [3 - 22] UMOL/L; CHLORIDE: 104 [100 - 110] MMOL/L; NPTST025-D-DIMER: 2527 [215 - 500] FEU NG/ML; NPTST067-QUALITATIVE SERUM PREGNANCY TES: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST082-TROPONIN: 0.01 [0 - 0.03] NG/ML; POTASSIUM: 3.9 [3.5 - 5.2] MMOL/L; SODIUM: 135 [135 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 103): CT SCAN OF ABDOMEN AND PELVIS:ARTERIAL EMBOLI LOCATED IN BILATERAL LUNG BASES, IN THE SEGMENTAL AND SUBSEGMENTAL ARTERIES; EKG:NORMAL SINUS RHYTHM

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Grade 4
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	REASONABLE POSSIBILITY THAT SAE IS RELATED TO IP.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING

Generated: [redacted]20[redacted]:14:15

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M19-944

治験責任医師からの報告。本被験者は米国の 3[redacted] 歳女性で，米国アッヴィ社の ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及びウパダシチニブが投与され，肺塞栓症を発現した。

Event 1 の臨床経過：

関連病歴は，裂孔ヘルニア，噴門形成術，慢性疲労，神経心臓性失神，軸性脊椎関節炎，甲状腺機能低下症，副腎機能不全，頻脈，非喫煙者及び非飲酒者であった。

被験者は 14 週時までは盲検化プラセボ対照期に参加していた。投与開始から 99 日後，ウパダシチニブの非盲検投与期に移行した。

投与開始から 103 日後，被験者は肺塞栓症を発現した。

投与開始から 101 日後，被験者は息切れの増悪及び頻脈を発現した。投与開始から 103 日後，被験者は悪心の症状で消化器科を受診し，続いて腹部及び骨盤部の CT スキャンを受けた。CT スキャンにて，両側性亜区域枝肺塞栓が認められた。CT 血管造影が行われた。同日，被験者は抗凝固療法のため入院した。入院時，被験者の治験薬及び経口避妊薬の投与は中止された。投与開始から 104 日後，被験者はエリキュース使用下で退院し，状態は安定していた。

治験責任医師は本事象に関連するリスク因子として，被験者の経口避妊薬の使用及び座りがちの生活を挙げた。

治験薬の投与は本事象のため中止された。

投与された薬剤は，エリキュース及びヘパリンであった。

The patient's past medications include:

NAPROSYN for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENBREL for AXIAL SPONDYLOARTHRITIS [redacted] 20[redacted] - [redacted] 20[redacted])

CELEBREX for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BELBUCA FILM for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DILAUDID for UNKNOWN INDICATION

GEODON for UNKNOWN INDICATION

VYVANSE for UNKNOWN INDICATION

MORPHINE for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.24.0] [10037377]

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

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

Dechallenge: Not Applicable

Causality for UPADACITINIB (Open Label)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.24.0] [10037377]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of PULMONARY EMBOLISM

- **Investigator:** Reasonable possibility that SAE is related to IP.

- **AbbVie:** Not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of PULMONARY EMBOLISM

- **Investigator:** Reasonable possibility that SAE is related to IP.

- **AbbVie:** Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BILIRUBIN:** 0.1 mg/dL (nmal 0.2 to 1.3)

[redacted] **20[redacted] CT SCAN:** Abdomen and pelvis: Arterial emboli located in bilateral lung bases, in the segmental and sub-segmental arteries.

[redacted] **20[redacted] D DIMER:** 2527.0 FEU NG/ML (normal 215.0 to 500.0)

[redacted] **20[redacted] EKG:** NORMAL SINUS RHYTHM.

[redacted] **20[redacted] QUALITATIVE SERUM PREGNANCY TEST:** Not detected.

[redacted] **20[redacted] TROPONIN:** >0.01 ng/ml

被験者番号 [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
帯状疱疹				X
リンパ球減少症				X
リンパ増殖性障害	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 15 MG QD /P2:ABT-494 15 MG QD	6[redacted]	FEMALE	ASIAN

Medical History	Onset Year
MEDICAL HISTORY: APPENDICITIS	19[redacted]
MEDICAL HISTORY: PSORIASIS VULGARIS	19[redacted]
MEDICAL HISTORY: MENOPAUSE	20[redacted]
MEDICAL HISTORY: CYSTITIS	20[redacted]
AXIAL SPONDYLOARTHRITIS DISEASE HISTORY: AXIAL SPONDYLOARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDICITOMY	19[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 mg	ORAL	QD	[redacted] / 1	[redacted] / 91	91
ABT-494	15 mg	ORAL	QD	[redacted] / 115	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
CALCIPOTRIOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
UREA	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
FOLIC ACID	5 mg	OTHER: 1 TIME PER WEEK	Y-M: 20[redacted] / -343
METHOTREXATE	5 mg	OTHER: 1 TIME PER WEEK	Y-M: 20[redacted] / -250
CELECOXIB	100 mg	BID	Y-M: 20[redacted] / -159
KETOPROFEN	NOT REPORTED	QD	Y-M: 20[redacted] / -159
LOXOPROFEN SODIUM	60 mg	TID	Y-M: 20[redacted] / -145
ETANERCEPT	50 mg	OTHER: 1 TIME PER WEEK	Y-M: 20[redacted] / -119
BETAMETHASONE BUTYRATE PROPIONATE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -107
LANSOPRAZOLE	15 mg	QD	Y-M: 20[redacted] / -82
PREDNISOLONE	3 mg	QD	Y-M: 20[redacted] / -82
LOXOPROFEN SODIUM	NOT REPORTED	2 TIMES PER WEEK	Y-M: 20[redacted] / -63
REBAMIPIDE	100 mg	OTHER: 2 TIMES PER WEEK	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
CALCIPOTRIOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]	NOT REPORTED
UREA	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	5 MG	OTHER: 1 TIME PER WEEK	Y-M: 20[redacted] / -343	NOT REPORTED

METHOTREXATE	5 MG	OTHER: 1 TIME PER WEEK	Y-M: 20[redacted] / -250	Y-M: 20[redacted] / 166
KETOPROFEN	NOT REPORTED	QD	Y-M: 20[redacted] / -159	NOT REPORTED
BETAMETHASONE BUTYRATE PROPIONATE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -107	NOT REPORTED
LANSOPRAZOLE	15 MG	QD	Y-M: 20[redacted] / -82	NOT REPORTED
PREDNISOLONE	3 MG	QD	Y-M: 20[redacted] / -82	NOT REPORTED
LOXOPROFEN SODIUM	NOT REPORTED	2 TIMES PER WEEK	Y-M: 20[redacted] / -63	NOT REPORTED
REBAMIPIDE	100 MG	OTHER: 2 TIMES PER WEEK	Y-M: 20[redacted] / -26	NOT REPORTED
RISEDRONATE SODIUM	17.5 MG	OTHER: 1 TIME PER WEEK	Y-M: 20[redacted] / 24	NOT REPORTED
FAMCICLOVIR	500 MG	TID	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 99
MECOBALAMIN	500 UG	TID	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 111
POLAPREZINC	75 MG	BID	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 111
ZINC	14 MG	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 150
BISACODYL	10 MG	OTHER: ONCE	Y-M: 20[redacted] / 135	Y-M: 20[redacted] / 135
MACROGOL 3350;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE	13 G	OTHER: ONCE	Y-M: 20[redacted] / 135	Y-M: 20[redacted] / 135
PARACETAMOL	200 MG	TID	Y-M: 20[redacted] / 140	Y-M: 20[redacted] / 143
SODIUM GUALENATE HYDRATE	5 ML	PRN	Y-M: 20[redacted] / 140	Y-M: 20[redacted] / 151
CEFCAPENE PIVOXIL HYDROCHLORIDE	100 MG	TID	Y-M: 20[redacted] / 144	Y-M: 20[redacted] / 146
DESLORATADINE	5 MG	QD	Y-M: 20[redacted] / 146	Y-M: 20[redacted] / 149
GARENOXACIN MESILATE	400 MG	QD	Y-M: 20[redacted] / 146	Y-M: 20[redacted] / 149
BETAMETHASONE	0.5 MG	BID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 151
DEXCHLORPHENIRAMINE MALEATE	4 MG	BID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 151
AMOXICILLIN TRIHYDRATE	750 MG	TID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 153
MONTELUKAST	10 MG	QD	Y-M: 20[redacted] / 151	Y-M: 20[redacted] / 163
LEVOFLOXACIN	500 MG	QD	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 163
SENNOSIDE A+B	24 MG	PRN	Y-M: 20[redacted] / 172	Y-M: 20[redacted] / 182
CEFCAPENE PIVOXIL HYDROCHLORIDE	100 MG	TID	Y-M: 20[redacted] / 317	Y-M: 20[redacted] / 322

Event #1: Event of Interest - Hematological Toxicity - Lymphopenia

Event Description	LYMPHOPENIA
Preferred Term	リンパ球減少症
AE Onset Date / Rx Day	[redacted]20[redacted] / 27
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	54
Duration of AE	28 DAYS
Severity	Grade 1
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Event of Interest - Hematological Toxicity - Lymphopenia

Event Description	LYMPHOPENIA
Preferred Term	リンパ球減少症
AE Onset Date / Rx Day	[redacted]20[redacted] / 55
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	

AE Stopped Rx Day	86
Duration of AE	32 DAYS
Severity	Grade 2
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #3: Event of Interest - Hematological Toxicity - Lymphopenia

Event Description	LYMPHOPENIA
Preferred Term	リンパ球減少症
AE Onset Date / Rx Day	[redacted]20[redacted] / 87
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	175
Duration of AE	89 DAYS
Severity	Grade 3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER
Preferred Term	帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 91
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Rx Day	99
Duration of AE	9 DAYS
Severity	Grade 1
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #5: Serious Adverse Event, Event of Interest - Malignancies

Event Description	OTHER IATROGENIC IMMUNODE FICIENCY-ASSOCIATED LYMPHOPROLIFERATIVE DISORDER.
Preferred Term	リンパ増殖性障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 167
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 167): LEUKOCYTES: 5.5 [4.3 - 7.3] 10^9/L; LYMPHOCYTES: 0.3 [1.1 - 3.3] 10^9/L; NPTST023-CRP: 3.1 [NOT REPORTED - 0.3] MG/DL; [redacted]20[redacted] (RX DAY 171): LEUKOCYTES: 5.7 [4.3 - 7.3] 10^9/L; LYMPHOCYTES: 1.3 [1.1 - 3.3] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 169): BLOOD ?-D GLUCAN: NEGATIVE; BLOOD ASPER ANTIGEN: NEGATIVE;
20[redacted] (RX DAY 171): BLOOD CMVANTIGEN(CS-HRP): POSITIVE-IT IS REACTIVATION OF CMV.; OTHER PULMONARY NODULES BIOPSY PULMONARY NODULES BIOPSY: NEGATIVE-CYTOLOGY?NO OBVIOUS ATYPIA IN LYMPHOCYTES.; [redacted]20[redacted] (RX DAY 176): OTHER CELL CULTURE CELL CULTURE: NEGATIVE-RESULTS OF CELL CULTURE SUBMITTED AT OTORHINOLARYNGOLOGY?NOT CLINICAL SIGNIFICANT.; BLOOD CMVANTIGEN(CS-HRP): NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 167): CHEST CT:MULTIPLE LUNG NODULE WAS CONFIRMED.

AE Stopped Rx Day	342
Duration of AE	176 DAYS
Severity	Grade 3
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]:14:15
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M19-944

治験責任医師からの報告。本被験者は日本の 6[redacted] 歳女性で，米国アッヴィ社の ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及びウパダシチニブが投与され，他の医原性免疫不全症関連リンパ増殖性疾患を発現した。

Event 5 の臨床経過：

関連病歴は，尋常性乾癬，閉経，脊椎関節炎，非喫煙者及び禁酒であった。

被験者は 14 週時までは盲検化プラセボ対照期に参加していた。投与開始から 115 日後，ウパダシチニブの非盲検投与期に移行した。

投与開始から 167 日後，他の医原性免疫不全症関連リンパ増殖性疾患を発現した。投与開始から 342 日後，他の医原性免疫不全症関連リンパ増殖性疾患は消失した。

投与開始から 167 日後，被験者は治験来院時，疲労，発熱，気力のなさ及び集中力のなさを訴えた。被験者は新型コロナウイルス感染症の疑いで救急治療室に運ばれた。胸部 CT 検査及び新型コロナウイルス PCR 検査が行われた。胸部 CT 検査にて多発性肺結節が認められた。投与開始から 169 日後，被験者は疲労のため入院した。投与開始から 171 日後までに，炎症反応は徐々に減少し，多発性肺結節は，軸性脊椎関節炎に対する薬剤に関連するリンパ増殖性障害が疑われた。投与開始から 176 日後，被験者は慢性咽頭痛のため耳鼻咽喉科を受診した。腫瘍形成は疑われなかった。投与開始から 188 日後，被験者の症状は改善し退院した。

投与開始から 202 日後，胸部 CT 検査が行われ，多発性肺結節の縮小が認められた。

治験責任医師によると，肺結節の大きさは不明であった。被験者に放射線被曝歴はなかった。更に，治験責任医師は，被験者に活動性結核の徴候がなく，本事象はサイトメガロウイルス感染によるものではないと報告した。結核やサルコイドーシスの精密検査は行われなかった。

The patient's past medications include:

CELECOX for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ETANERCEPT BS for AXIAL SPONDYLOARTHRITIS [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Lymphoproliferative disorder (10061232) (Lymphoproliferative disorder (10061232)) [v.24.0] [10061232]

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

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

Dechallenge: Not Applicable

Causality for UPADACITINIB (Open Label)

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1) Lymphoproliferative disorder (10061232) (Lymphoproliferative disorder (10061232)) [v.24.0] [10061232]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of OTHER IATROGENIC IMMUNODEFICIENCY-ASSOCIATED LYMPHOPROLIFERATIVE DISORDER

- **Investigator:** Not applicable

- **AbbVie:** Not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of OTHER IATROGENIC IMMUNODEFICIENCY-ASSOCIATED LYMPHOPROLIFERATIVE DISORDER

- **Investigator:** Not applicable

- **AbbVie:** Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ASPER ANTIGEN:** Negative

[redacted] 20[redacted] **B-D GLUCAN:** Negative

[redacted] 20[redacted] **BODY TEMPERATURE:** 38 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 37.7 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 36.4 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 36.8 Degrees C

[redacted] 20[redacted] **BODY WEIGHT:** 43.8 KG

[redacted] 20[redacted] **BRONCHOSCOPY:** A few cells with mild nuclear swelling were confirmed.

[redacted] 20[redacted] **CELL CULTURE:** Not clinically significant.

[redacted] 20[redacted] **CHEST CT:** Multiple lung nodule

[redacted] 20[redacted] **CHEST CT:** Multiple nodules became smaller.

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

[redacted] 20[redacted] **CMV ANTIGEN (CS-HRP):** (Blood specimen) Positive. Reactivation of CMV

[redacted] 20[redacted] **CMV ANTIGEN (CS-HRP):** (Blood specimen) Negative

[redacted] 20[redacted] **COVID-19 PCR:** Negative

[redacted] 20[redacted] **CRP:** 3.1 mg/dL

[redacted] 20[redacted] **CRP:** 10.53 mg/dL

[redacted] 20[redacted] **CRP:** 7.52 mg/dL

[redacted] 20[redacted] **CRP:** 0.08 mg/dL

[redacted] 20[redacted] **CELL CULTURE:** Results of cell culture submitted at otorhinolaryngology: not clinical significant.

[redacted] 20[redacted] **HBV-DNA:** Negative

[redacted] 20[redacted] **PULMONARY NODULES BIOPSY:** Cytology: No obvious atypia in lymphocytes.(Negative)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes zoster: Involving T2, T3, T4, and T5. Study drug interrupted.
Lymphopenia [redacted] 20[redacted]): Study drug interrupted.

被験者番号 [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
播種性水痘帯状疱疹ウイルス感染	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO /P2:ABT-494 15 MG QD	6[redacted]	MALE	ASIAN

Medical History	Onset Year
MEDICAL HISTORY: VARICELLA	19[redacted]
MEDICAL HISTORY: CHORONIC TONSILLITIS	19[redacted]
MEDICAL HISTORY: DIABATES	19[redacted]
MEDICAL HISTORY: CHRONIC RHINITIS	20[redacted]
MEDICAL HISTORY: CRAMPS IN THE CALVES	20[redacted]
MEDICAL HISTORY: DYSLIPIDEMIA	20[redacted]
MEDICAL HISTORY: HYPERTENSION	20[redacted]
AXIAL SPONDYLOARTHRITIS DISEASE HISTORY: AXIAL SPONDYLOARTHRITIS	20[redacted]
MEDICAL HISTORY: EDEMA OF LEFT UPPER AND LOWER LIMBS	20[redacted]
MEDICAL HISTORY: MICROSCOPIC HEMATURIA	20[redacted]
MEDICAL HISTORY: PROTEINURIA	20[redacted]
MEDICAL HISTORY: LACUNAR INFARCTION	20[redacted]
MEDICAL HISTORY: CHRONIC GASTRITIS	20[redacted]
MEDICAL HISTORY: GINGIVITIS	20[redacted]
MEDICAL HISTORY: CONTACT DERMATITIS	20[redacted]
MEDICAL HISTORY: 1ST DEGREE ATRIOVENTRICULAR BLOCK	20[redacted]
MEDICAL HISTORY: LEFT ARTERIOR FASCICULAR BLOOK	20[redacted]
MEDICAL HISTORY: CATARACT	20[redacted]
MEDICAL HISTORY: BULLA ON RIGHT APITAL LUNG	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: TONSILLAR SURGERY	19[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	30 CIGARETTE	41	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted] / 1	[redacted] / 94	94
ABT-494	15 mg	ORAL	QD	[redacted] / 95	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BENZETHONIUM CHLORIDE;CHLORPHENAMINE MALEATE;NAPHAZOLINE HYDROCHLORIDE	1 OTHER: PUFFS	PRN	Y-M: 20[redacted]
LOXOPROFEN SODIUM	60 mg	PRN	Y-M: 20[redacted]
KETOPROFEN	NOT REPORTED	QD	Y-M: 20[redacted]
REBAMIPIDE	100 mg	BID	Y-M: 20[redacted]
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted]
CELECOXIB	200 mg	BID	Y-M: 20[redacted]
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted]
VALSARTAN	80 mg	QD	Y-M: 20[redacted]
LINAGLIPTIN	5 mg	QD	Y-M: 20[redacted]
METFORMIN HYDROCHLORIDE	500 mg	QID	Y-M: 20[redacted]
ESOMEPRAZOLE MAGNESIUM	20 mg	QD	Y-M: 20[redacted]
INTERLEUKINS	210 mg	OTHER: ONCE EVERY 2WEEKS	Y-M: 20[redacted]
SECUKINUMAB	150 mg	OTHER: ONCE EVERY 4 WEEKS	Y-M: 20[redacted] / -298
DICLOFENAC SODIUM	NOT REPORTED	BID	Y-M: 20[redacted] / -207
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / -127
PEMAFIBRATE	0.1 mg	BID	Y-M: 20[redacted] / -127

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
BENZETHONIUM CHLORIDE;CHLORPHENAMINE MALEATE;NAPHAZOLINE HYDROCHLORIDE	1 OTHER: PUFFS	PRN	Y-M: 20[redacted]	NOT REPORTED
KETOPROFEN	NOT REPORTED	QD	Y-M: 20[redacted]	NOT REPORTED
REBAMIPIDE	100 MG	BID	Y-M: 20[redacted]	NOT REPORTED
SULFASALAZINE	500 MG	BID	Y-M: 20[redacted]	NOT REPORTED
VALSARTAN	80 MG	QD	Y-M: 20[redacted]	NOT REPORTED
LINAGLIPTIN	5 MG	QD	Y-M: 20[redacted]	NOT REPORTED
METFORMIN HYDROCHLORIDE	500 MG	QID	Y-M: 20[redacted]	NOT REPORTED
ESOMEPRAZOLE MAGNESIUM	20 MG	QD	Y-M: 20[redacted]	NOT REPORTED
DICLOFENAC SODIUM	NOT REPORTED	BID	Y-M: 20[redacted] / -207	Y-M: 20[redacted] / 471
AMLODIPINE	5 MG	QD	Y-M: 20[redacted] / -127	NOT REPORTED
PEMAFIBRATE	0.1 MG	BID	Y-M: 20[redacted] / -127	NOT REPORTED
MAGNESIUM OXIDE	330 MG	TID	Y-M: 20[redacted] / 123	NOT REPORTED
ROSUVASTATIN	2.5 MG	QD	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 454
TOZINAMERAN	NOT REPORTED	ONCE	Y-M: 20[redacted] / 440	Y-M: / 440
BETAMETHASONE BUTYRATE PROPIONATE	1 OTHER: APPLICATION	QID	Y-M: 20[redacted] / 445	Y-M: 20[redacted] / 446
DICLOFENAC SODIUM	NOT REPORTED	QD	Y-M: 20[redacted] / 445	Y-M: 20[redacted] / 471
TOZINAMERAN	NOT REPORTED	ONCE	Y-M: 20[redacted] / 461	Y-M: / 461
VALACICLOVIR	1000 MG	TID	Y-M: 20[redacted] / 466	Y-M: 20[redacted] / 468
VIDARABINE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 466	Y-M: 20[redacted] / 468
HYDROCORTISONE;OXYTETRACYCLINE HYDROCHLORIDE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 469	NOT REPORTED
PARACETAMOL	200 MG	TID	Y-M: 20[redacted] / 469	Y-M: 20[redacted] / 470
ACICLOVIR	750 MG	BID	Y-M: 20[redacted] / 469	Y-M: 20[redacted] / 474
PARACETAMOL;TRAMADOL HYDROCHLORIDE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 469	Y-M: 20[redacted] / 474

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

Event Description	HERPES ZOSTER DISSEMINATED
Preferred Term	播種性水痘帯状疱疹ウイルス感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 463
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Grade 3
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]:14:15
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M19-944

治験責任医師からの報告。本被験者は日本の 6[redacted] 歳男性で，米国アッヴィ社の ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及びウパダシチニブが投与され，播種性帯状疱疹を発現した。

Event 1 の臨床経過：

関連病歴は，水痘，糖尿病，慢性鼻炎，接触性皮膚炎，喫煙者（1 日 30 本を 41 年間）及び禁酒であった。

被験者は 14 週時までは盲検化プラセボ対照期に参加していた。投与開始から 95 日後，ウパダシチニブの非盲検投与期に移行した。

投与開始から 463 日後，被験者は播種性帯状疱疹を発現した。

投与開始から 461 日後，本事象の発現に先立ち，被験者の左腕内側に発疹が認められた。投与開始から 466 日後，発疹は水疱と疼痛の悪化を伴い，左腕内側，顔及び背部全体に広がった。被験者によると発熱はなく，近医を受診し帯状疱疹と診断された。被験者にビダラビン及びバラシクロビルの投与が開始された。投与開始から 468 日後，治験薬の投与は中止された。

投与開始から 469 日後，被験者は播種性帯状疱疹の診断にて，鎮痛剤及びアシクロビル静脈注射による院内治療のため入院した。投与開始から 473 日後，発疹は痂皮化したように見え，疼痛は緩和した。バイタルサインは安定してきており発熱はなかった。投与開始から 475 日後，被験者は退院した。

治験責任医師によると，被験者には水痘歴があり，帯状疱疹ワクチンは接種していなかった。身体検査及び病歴から診断された。左側 V1，V2，V3，T1，T2，T3，L2，L4 及び右側 V1，T2，L2 を含む多数のデルマトームから発疹は確認された。

投与された薬剤は，プレガバリン，アシクロビル，アズノール，ナウゼリン，メトクロプラミド，トラマール，テラ・コートリル，トアラセット，アセトアミノフェン，アシクロビル，バラシクロビル及びビダラビンであった。

The patient's past medications include:

LOXONIN for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CELECOX for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMAN INTERLOKIN 17 RECEPTOR FULLY HUMAN ANTIBODY TO RECEPTOR A for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COSENTYX for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster disseminated (10065038) (Disseminated varicella zoster virus infection (10084396)) [v.24.0] [10065038]

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

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

Dechallenge: Not Applicable

Causality for UPADACITINIB (Open Label)

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1) Herpes zoster disseminated (10065038) (Disseminated varicella zoster virus infection (10084396)) [v.24.0] [10065038]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of HERPES ZOSTER DISSEMINATED

- **Investigator:** Not applicable

- **AbbVie:** Not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of HERPES ZOSTER DISSEMINATED

- **Investigator:** Not applicable

- **AbbVie:** Not applicable

被験者番号 [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
多発性外傷	X		X	

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO /P2:ABT-494 15 MG QD	4[redacted]	MALE	WHITE

Medical History	Onset Year
AXIAL SPONDYLOARTHRITIS DISEASE HISTORY: AXIAL SPONDYLOARTHRITIS	20[redacted]
MEDICAL HISTORY: GENERALIZED OSTEOARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
NOT REPORTED	

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 103	103
ABT-494	15 mg	ORAL	QD	[redacted]20[redacted] / 104	[redacted]20[redacted] / 249	146

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY 2 WEEKS	Y-M: 20[redacted]
ETODOLAC	400 mg	BID	Y-M: 20[redacted]
DICLOFENAC SODIUM	75 mg	QD	Y-M: 20[redacted] / -315
TOLPERISONE HYDROCHLORIDE	150 mg	BID	Y-M: 20[redacted] / -315
BENFOTIAMINE;CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE	1 OTHER: CAPSULE	BID	Y-M: 20[redacted] / -38
PANTOPRAZOLE SODIUM SESQUIHYDRATE	40 mg	PRN	Y-M: 20[redacted] / -38
TOLPERISONE HYDROCHLORIDE	150 mg	TID	Y-M: 20[redacted] / -38

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BENFOTIAMINE;CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE	1 OTHER: CAPSULE	BID	Y-M: 20[redacted] / -38	Y-M: 20[redacted] / 249
PANTOPRAZOLE SODIUM SESQUIHYDRATE	40 MG	PRN	Y-M: 20[redacted] / -38	Y-M: 20[redacted] / 249
TOLPERISONE HYDROCHLORIDE	150 MG	TID	Y-M: 20[redacted] / -38	Y-M: 20[redacted] / 249

Event #1: Serious Adverse Event, Death

Event Description POLYTRAUMA

Preferred Term 多発性外傷

AE Onset Date / Rx Day [redacted]20[redacted] / 249

Age at AE Onset 4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	249
Duration of AE	1 DAY
Severity	Grade 5
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUICIDAL INTENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	LIFE THREATENING, DEATH OF SUBJECT

Generated: [redacted] 20[redacted]:14:15

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M19-944

治験責任医師からの報告。本被験者はブルガリアの 4[redacted] 歳男性で，米国アッヴィ社の ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及びウパダシチニブが投与され，致死性多発外傷を発現した。

Event 1 の臨床経過：

関連病歴は，軸性脊椎関節炎，非喫煙者及び非飲酒者であった。

被験者は 14 週時までは盲検化プラセボ対照期に参加していた。投与開始から 104 日後，ウパダシチニブの非盲検投与期に移行した。

投与開始から 249 日後，被験者は多発外傷を発現した。同日，被験者は死亡した。死因は多発外傷と報告された。剖検の実施の有無は不明であった。

治験責任医師によると，最終来院日の投与開始から 243 日後には本事象に関連する徴候や症状は被験者に認められなかった。投与開始から 251 日後，警察が治験責任医師に，投与開始から 249 日後被験者は自殺したと報告した。警察によると，死因は非常に高い場所から意図的に飛び降りたことであった。死亡証明書の入手はなかった。

The patient's past medications include:

HUMIRA for AXIAL SPONDYLOARTHRITIS([redacted] 20[redacted] - [redacted] 20[redacted])

ETODIN FORT for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ALMIRAL for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Polytrauma (10080245) (Multiple injuries (10028224)) [v.24.0] [10080245]

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

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

Dechallenge: Not Applicable

Causality for UPADACITINIB (Open Label)

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1) Polytrauma (10080245) (Multiple injuries (10028224)) [v.24.0] [10080245]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of POLYTRAUMA

- **Investigator:** suicidal intent

- **AbbVie:** The event of polytrauma is most likely due to an intentional fall from a great height as according to the police as noted in the narrative.

Alternative Etiology for UPADACITINIB (Open Label)

Event of POLYTRAUMA

- **Investigator:** suicidal intent

- **AbbVie:** The event of polytrauma is most likely due to an intentional fall from a great height as according to the police as noted in the narrative.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
COVID-19	X			X
COVID-19 肺炎	X			X
胆石症	X			
胆汁うっ滞性黄疸				X

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 15 MG QD /P2:ABT-494 15 MG QD	3[redacted]	MALE	WHITE

Medical History	Onset Year
AXIAL SPONDYLOARTHRITIS DISEASE HISTORY: AXIAL SPONDYLOARTHRITIS	20[redacted]
MEDICAL HISTORY: CHRONIC BACK PAIN	20[redacted]
MEDICAL HISTORY: OSTEOPOROSIS	20[redacted]
MEDICAL HISTORY: HYPERURICEMIA	20[redacted]
MEDICAL HISTORY: SINUS BRADYCARDIA	20[redacted]

Prior Procedures	Procedure Year
NOT REPORTED	

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	LESS THAN 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 99	99
ABT-494	15 mg	ORAL	QD	[redacted]20[redacted] / 100	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
IBUPROFEN	400 mg	TID	Y-M: 20[redacted]
IBUPROFEN	600 mg	TID	Y-M: 20[redacted]
SECUKINUMAB	150 mg	OTHER: MONTHLY	Y-M: 20[redacted]
ALLOPURINOL	100 mg	QD	Y-M: 20[redacted]
CALCIUM CARBONATE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -278
NIMESULIDE	100 mg	QD	Y-M: 20[redacted] / -278
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -159

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
ALLOPURINOL	100 MG	QD	Y-M: 20[redacted]	NOT REPORTED
CALCIUM CARBONATE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -278	NOT REPORTED
CEFUROXIME AXETIL	500 MG	BID	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 56
CODEINE PHOSPHATE	15 MG	TID	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 56
SALBUTAMOL	100 UG	PRN	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 56
POTASSIUM CHLORIDE	7.45%	PRN	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 61
AMBROXOL HYDROCHLORIDE	15 MG	PRN	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 64
AMINOPHYLLINE	24 OTHER: MG/ML	PRN	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 64
AMOXICILLIN;CLAVULANIC ACID	1 OTHER: INFUSION	TID	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 64
CLARITHROMYCIN	500 MG	BID	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 64
ERDOSTEINE	300 MG	PRN	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 64

GLUCONATE SODIUM;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 ML	PRN	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 64
HYDROCORTISONE	100 MG	PRN	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 64
IPRATROPIUM BROMIDE	0.020 MG	PRN	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 64
SIMETICONE	40 MG	PRN	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 64
AMOXICILLIN;CLAVULANIC ACID	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 70
CLARITHROMYCIN	500 MG	BID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 71
ACETYLCYSTEINE	600 MG	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 75
LACTOBACILLUS ACIDOPHILUS	2 OTHER: TABLET	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 78
AMOXICILLIN TRIHYDRATE;CLAVULANATE POTASSIUM	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 353
BISULEPIN HYDROCHLORIDE	2 MG	PRN	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 353
CEFOPERAZONE SODIUM	2 G	BID	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 353
NADROPARIN CALCIUM	0.6 ML	QD	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 353
IOMEPROL	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted] / 346	Y-M: 20[redacted] / 346
BROMAZEPAM	3 MG	PRN	Y-M: 20[redacted] / 380	Y-M: 20[redacted] / 383
GLUCONATE SODIUM;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	1000 ML	PRN	Y-M: 20[redacted] / 380	Y-M: 20[redacted] / 383
METAMIZOLE SODIUM	500 MG	PRN	Y-M: 20[redacted] / 380	Y-M: 20[redacted] / 383
NADROPARIN CALCIUM	0.4 ML	QD	Y-M: 20[redacted] / 380	Y-M: 20[redacted] / 383
PARACETAMOL	1 G	PRN	Y-M: 20[redacted] / 380	Y-M: 20[redacted] / 383

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

Event Description	COVID-19 INFECTION
Preferred Term	COVID-19
AE Onset Date / Rx Day	[redacted]20[redacted] / 50
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 57): C REACTIVE PROTEIN: 225 [0 - 5] MG/L; POTASSIUM: 3.2 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 59): C REACTIVE PROTEIN: 112.2 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 61): C REACTIVE PROTEIN: 64.2 [0 - 5] MG/L; POTASSIUM: 3.7 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 65): C REACTIVE PROTEIN: 11.2 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 57): CHEST X-RAY:BILATERAL BRONCHOPNEUMONIA; OXYGENTHERAPY FROM [redacted]20[redacted] TO [redacted]20[redacted] AS PER NEEDED.:CONDITION IMPROVED; [redacted]20[redacted] (RX DAY 65): CHEST X-RAY:MULTIPLE PULMONARY INFILTRATES, MORE IN THE RIGHT WING, IN COMPARISON WITH THE EXAMINATION [redacted]/20[redacted] REGRESSION OF THE FINDING

AE Stopped Rx Day	82
Duration of AE	33 DAYS
Severity	Grade 3
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

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

Event Description	COVID-19 BILATERAL BRONCHOPNEUMONIA
Preferred Term	COVID-19 肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 50
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 57): C REACTIVE PROTEIN: 225 [0 - 5] MG/L; POTASSIUM: 3.2 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 59): C REACTIVE PROTEIN: 112.2 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 61): C REACTIVE PROTEIN: 64.2 [0 - 5] MG/L; POTASSIUM: 3.7 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 65): C REACTIVE PROTEIN: 11.2 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 57): CHEST X-RAY:BILATERAL BRONCHOPNEUMONIA; OXYGENTHERAPY FROM

[redacted]20[redacted] TO [redacted]20[redacted] AS PER NEEDED.:CONDITION IMPROVED; [redacted]20[redacted] (RX DAY 65): CHEST X-RAY:MULTIPLE PULMONARY INFILTRATES, MORE IN THE RIGHT WING, IN COMPARISON WITH THE EXAMINATION [redacted]/20[redacted] REGRESSION OF THE FINDING

AE Stopped Rx Day	82
Duration of AE	33 DAYS
Severity	Grade 3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID-19 INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	CHOLECYSTOLITHIASIS
Preferred Term	胆石症
AE Onset Date / Rx Day	[redacted]20[redacted] / 341
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 344): ALANINE AMINOTRANSFERASE: 770 [0 - 44] U/L; ASPARTATE AMINOTRANSFERASE: 392 [0 - 40] U/L; NPTST009-BIL-D: 45.3 [0 - 5.1] UMOL/L; NPTST010-BIL-T: 112.1 [0 - 17] UMOL/L; NPTST023-CRP: 2.5 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 346): ALANINE AMINOTRANSFERASE: 644 [0 - 44] U/L; ASPARTATE AMINOTRANSFERASE: 221 [0 - 40] U/L; NPTST009-BIL-D: 30.6 [0 - 5.1] UMOL/L; NPTST010-BIL-T: 80.9 [0 - 17] UMOL/L; [redacted]20[redacted] (RX DAY 351): ALANINE AMINOTRANSFERASE: 298 [0 - 44] U/L; ASPARTATE AMINOTRANSFERASE: 87 [0 - 40] U/L; NPTST009-BIL-D: 15.2 [0 - 5.1] UMOL/L; NPTST010-BIL-T: 44.4 [0 - 17] UMOL/L; [redacted]20[redacted](RX DAY 353): ALANINE AMINOTRANSFERASE: 214 [0 - 44] U/L; ASPARTATE AMINOTRANSFERASE: 65 [0 - 40] U/L; NPTST009-BIL-D: 12.5 [0 - 5.1] UMOL/L; NPTST010-BIL-T: 45 [0 - 17] UMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 381): OTHER GALLBLADDER CONTENT CULTURE EXAMINATION: NEGATIVE-WITHOUT BACTERIAL GROWTH; OTHER GALLBLADDER CONTENT CULTURE EXAMINATION: NEGATIVE-CULTIVATION FOR YEAST NEGATIVE; OTHER GALLBLADDER CONTENT MICROSCOPIC EXAM OF GALLBLADDER: NEGATIVE-INFLAMMATORY CELLS NOT FOUND, MICROBES NOT FOUND

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 344): ULTRASOUND OF ABDOMEN:LIVER NOT ENLARGED, WITH REGULAR STRUCTURE, WITHOUT BILE DUCT DILATATION, GALLBLADDER MORE VOLUMINOUS, GLACIAL WIDTH 4 CM, WITHOUT STONES. DUCTUS CHOLEDUS NOT DILATED. NO SIGNIFICANT PATHOLOGICAL CHAN; X-RAY OF ABDOMEN:WITHOUT SIGNS OF GIT PERFORATION OR ILEOSIS IN X-RAY, CHOLECYSTOLITHIASIS; [redacted]20[redacted] (RX DAY 346): CHEST X-RAY:LEFT SUBHILOSOPHICALLY PARACARDIACAL STRIPE PATTERN, NOW WITHOUT FRESH INFILTRATION IN THE LUNG PARENCHYMA; CT OF ABDOMEN:POSTINFILTRATIVE DRAWING OF THE LUNG ON THE LEFT, CHOLEDOCHOLITHIASIS MULTIPLEX, SLIGHT DILATATION OF THE CHOLEDOCHUS ON THE BASIS OF SUPRAPAPILLARY CHOLEDOCHOLITIASIS; [redacted]20[redacted] (RX DAY 351): CHEST X-RAY:FURTHER REGRESSION ON THE LEFT LUNG, SUBHILOSOPHICALLY PRONOUNCED REGRESSION OF THE STRIPE PATTERN, THE REST OF THE LUNG IS FREE; [redacted]20[redacted] (RX DAY 352):

ENDOSCOPIC PAPILLOSPHINCTEROTOMY:WITHOUT LITHIASIS GAIN; ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY:UNDILATED BILE TREE; [redacted]20[redacted] (RX DAY 381): LAPAROSCOPIC CHOLECYSTECTOMY:OPEN GALLBLADDER DIAMETER 30X70 MM, STONES - SMALL CRUMB TOTAL DIAMETER 5 MM, COARSE MUCOSA

AE Stopped Rx Day	383
Duration of AE	43 DAYS
Severity	Grade 3
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

Event #4: Event of Interest - Drug Related Hepatic Disorders

Event Description	OBSTRUCTIVE JAUNDICE
Preferred Term	胆汁うっ滞性黄疸
AE Onset Date / Rx Day	[redacted]20[redacted] / 341
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	353
Duration of AE	13 DAYS
Severity	Grade 2
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:14:15

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M19-944

治験責任医師からの報告。本被験者はチェコ共和国の 3[redacted]歳男性で，米国アッヴィ社の ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，新型コロナウイルス感染症及び新型コロナウイルス両側気管支肺炎を発現した。

Event 1 及び 2 の臨床経過：

関連病歴は，骨粗鬆症，高尿酸血症，洞性徐脈，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

投与開始から 50 日後，被験者は新型コロナウイルス感染症及び新型コロナウイルス両側気管支肺炎を発現した。投与開始から 82 日後，新型コロナウイルス感染症及び新型コロナウイルス両側気管支肺炎は消散した。

投与開始から 50 日後から，被験者は呼吸困難，乾性咳嗽，下痢及び夜間発熱を発現した。投与開始から 57 日後，被験者は状態悪化のため入院した。胸部 X 線検査にて両側気管支肺炎が認められた。投与開始から 57 日後，新型コロナウイルスに対する PCR 検査が実施され，陽性が確認された。被験者は抗生物質及び粘液溶解薬の治療を受けた。被験者は集中治療室に収容され，酸素投与された。被験者の状態は改善し，胸部 X 線検査にて浸潤の退縮が認められた。投与開始から 65 日後，被験者は発熱もなく良好な状態で退院し，自宅における抗生物質治療を継続した。投与開始から 71 日後，被験者は抗生物質治療を完了した。投与開始から 75 日後から，被験者に咳や呼吸困難の徴候は認められなかった。投与開始から 82 日後，呼吸器科で検査が実施され，肺胞呼吸に副雑音は認められなかった。胸部 X 線検査により，退行性変化のみられる肺炎で浸潤の退縮が認められた。被験者の体調は良好であった。

治験責任医師によると，被験者にリスク因子はなかった。

投与された薬剤は，ambrobene，コデイン，ventolin，erdomed，klacid，atroent N，espumisan，plasmalyte，ヒドロコルチゾン，syntophyllin，アセチルシステイン，xorimax 及び amoksiklav であった。

The patient's past medications include:

BRUFEN for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

COSENTYX for AXIAL SPONDYLOARTHRITIS [redacted] 20[redacted] - [redacted] 20[redacted])

AULIN for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MELOXIKAM for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) COVID-19 (10084268) (COVID-19 (10084268)) [v.24.0] [10084268]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.24.0] [10084380]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID-19 INFECTION

- **Investigator:** Unknown

- **AbbVie:** Event is more likely related to the COVID-19 pandemic outbreak.

Event of COVID-19 BILATERAL BRONCHOPNEUMONIA

- **Investigator:** COVID-19 infection.

- **AbbVie:** Event is more likely related to the concurrent COVID-19 infection.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** BILATERAL BRONCHOPNEUMONIA

[redacted] **20[redacted] CHEST X-RAY:** MULTIPLE PULMONARY INFILTRATES, MORE IN THE RIGHT WING, IN COMPARISON WITH THE EXAMINATION [redacted]/20[redacted] REGRESSION OF THE FINDING

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

[redacted] **20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN:** 225.0 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN:** 112.2 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN:** 64.2 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted] HIGH-SENSITIVITY C REACTIVE PROTEIN:** 11.2 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted] POTASSIUM:** 3.2 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] POTASSIUM:** 3.7 MMOL/L (normal 3.5 to 5.1)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M19-944

治験責任医師からの報告。本被験者はチェコ共和国の 3[redacted] 歳男性で，米国アッヴィ社の ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及びウパダシチニブが投与され，胆嚢結石症を発現した。

Event 3 の臨床経過：

関連病歴は，軸性脊椎関節炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

被験者は投与 14 週時までは盲検下プラセボ対照期に参加していた。投与開始から 100 日後，被験者はウパダシチニブの非盲検投与期に移行した。

投与開始から 341 日後，被験者は胆嚢結石症を発現した。投与開始から 383 日後，胆嚢結石症は消失した。

入院前の投与開始から 341 日後，被験者は腹痛，悪心及び黄染を発現した。投与開始から 344 日後，被験者は入院し，閉塞性黄疸（非重篤）及び胆嚢結石症と診断された。被験者は抗生物質（詳細不明）による治療を受けた。投与開始から 352 日後，内視鏡的逆行性胆道膵管造影及び内視鏡的乳頭括約筋切開術が行われ，結石症は認められなくなった。投与開始から 353 日後，被験者は退院した。

投与開始から 380 日後，被験者は胆嚢結石症の悪化のため再入院した。投与開始から 381 日後，腹腔鏡下胆嚢摘出術が行われた。治験薬の投与は中止された。投与開始から 383 日後，被

験者は良好な状態で退院した。投与開始から 393 日後，被験者は外科で検査を受けた。縫合糸は抜糸され，手術創は良好な状態と判断された。
投与された薬剤は，lexaurin，dithiaden，amoksiklav，acefa，fraxiparine，plasmalyte，パラセタモール及び novalgin であった。

The patient's past medications include:

BRUFEN for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

COSENTYX for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AULIN for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MELOXIKAM for AXIAL SPONDYLOARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Cholecystolithiasis (10049890) (Cholelithiasis (10008629)) [v.24.0] [10049890]

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

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

Dechallenge: Not Applicable

Causality for UPADACITINIB (Open Label)

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1) Cholecystolithiasis (10049890) (Cholelithiasis (10008629)) [v.24.0] [10049890]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of CHOLECYSTOLITHIASIS

- **Investigator:** Unknown

- **AbbVie:** Cholelithiasis is a common event in the general population with prevalence of gallstones in non-Hispanic white men of 8.6%. Additional risk factors includes obesity and hyperuricemia.

Alternative Etiology for UPADACITINIB (Open Label)

Event of CHOLECYSTOLITHIASIS

- **Investigator:** Cholecystolithiasis.

- **AbbVie:** Cholelithiasis is a common event in the general population with prevalence of gallstones in non-Hispanic white men of 8.6%. Additional risk factors includes obesity and hyperuricemia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 12.83 ukat/L (normal 0 to 0.73)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 10.73 ukat/L (normal 0 to 0.73)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 4.96 ukat/L (normal 0 to 0.73)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 3.57 umol/L (normal 0 to 0.73)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 1.09 ukat/L (normal 0 to 0.67)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 6.54 ukat/L (normal 0 to 0.67)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 3.68 ukat/L (normal 0 to 0.67)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 1.45 ukat/L (normal 0 to 0.67)

[redacted] **20[redacted] BIL-D:** 45.3 umol/L (normal 0 to 5.1)

[redacted] **20[redacted] BIL-D:** 30.6 umol/L (normal 0 to 5.1)

[redacted] 20[redacted] **BIL-D:** 15.2 umol/L (normal 0 to 5.1)

[redacted] 20[redacted] **BIL-D:** 12.5 umol/L (normal 0 to 5.1)

[redacted] 20[redacted] **BIL-T:** 112.1 umol/L (normal 0 to 17)

[redacted] 20[redacted] **BIL-T:** 80.9 umol/L (normal 0 to 17.0)

[redacted] 20[redacted] **BIL-T:** 44.4 umol/L (normal 0 to 17.0)

[redacted] 20[redacted] **BIL-T:** 45 umol/L (normal 0 to 17.0)

[redacted] 20[redacted] **BMI:** 30.2 kg/m2

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 2.5 MG/L (normal 0 to 5.0)

[redacted] 20[redacted] **CHEST X-RAY:** Left subhilosophically paracardiacal stripe pattern, now without fresh infiltration in the lung parenchyma.

[redacted] 20[redacted] **CHEST X-RAY:** Further regression on the left lung, subhilosophically pronounced regression of the stripe pattern, the rest of the lung is free.

[redacted] 20[redacted] **CT OF ABDOMEN:** Postinfiltrative drawing of the lung on the left, choledocholithiasis multiplex, slight Dilatation of the choledochus on the basis of suprapapillary choledocholitiasis.

[redacted] 20[redacted] **CULTURE:** Culture examination: gallbladder content was negative, without bacterial growth, cultivation for yeast was negative

[redacted] 20[redacted] **ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY:** Undilated bile tree.

[redacted] 20[redacted] **LIVER FUNCTION TEST:** Decreased.

[redacted] 20[redacted] **MICROSCOPY:** Microscopic Exam of gallbladder content was negative - inflammatory cells not found, microbes not found

[redacted] 20[redacted] **ULTRASOUND OF ABDOMEN:** LIVER NOT ENLARGED, WITH REGULAR STRUCTURE, WITHOUT BILE DUCT DILATATION, GALLBLADDER MORE VOLUMINOUS, GLACIAL WIDTH 4 CM, WITHOUT STONES. DUCTUS CHOLEDUS NOT DILATED. NO SIGNIFICANT PATHOLOGICAL CHANGES

[redacted] 20[redacted] **X-RAY OF ABDOMEN:** Without signs of git perforation or ileosis in X-ray, cholecystolithiasis.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
COVID-19	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:PLACEBO /P2:ABT-494 15 MG QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
AXIAL SPONDYLOARTHRITIS DISEASE HISTORY: AXIAL SPONDYLOARTHRITIS	20[redacted]
MEDICAL HISTORY: BRONCHIAL ASTHMA	20[redacted]
MEDICAL HISTORY: LYME BORRELIOSIS SKIN FORM	20[redacted]
MEDICAL HISTORY: LYME BORRELIOSIS SKIN FORM	20[redacted]
MEDICAL HISTORY: SEBORRHEIC DERMATITIS	20[redacted]
MEDICAL HISTORY: MENOPAUSE	20[redacted]
MEDICAL HISTORY: OBESITY	20[redacted]
MEDICAL HISTORY: POLYNEUROPATHY OF THE LOWER LIMBS	20[redacted]
MEDICAL HISTORY: GASTROESOPHAGEAL REFLUX	20[redacted]
MEDICAL HISTORY: TONSILLITIS BILATERALLY	20[redacted]
MEDICAL HISTORY: URINARY TRACT INFECTIONS	20[redacted]

Prior Procedures	Procedure Year
NOT REPORTED	

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 98	98
ABT-494	15 mg	ORAL	QD	[redacted]20[redacted] / 99	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
IBUPROFEN	400 mg	TID	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
DICLOFENAC SODIUM	75 mg	BID	Y-M: 20[redacted]
CICLESONIDE	160 ug	QD	Y-M: 20[redacted]
SALBUTAMOL	100 ug	PRN	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted]
NIMESULIDE	NOT REPORTED	BID	Y-M: 20[redacted] / -69

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SULFASALAZINE	1000 MG	BID	Y-M: 20[redacted]	NOT REPORTED
OMEPRAZOLE	20 MG	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 266
CICLESONIDE	160 UG	QD	Y-M: 20[redacted]	NOT REPORTED
SALBUTAMOL	100 UG	PRN	Y-M: 20[redacted]	NOT REPORTED
NIMESULIDE	NOT REPORTED	BID	Y-M: 20[redacted] / -69	NOT REPORTED
PARACETAMOL	500 MG	PRN	Y-M: 20[redacted] / 123	NOT REPORTED

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

Event Description	COVID-19 INFECTION
Preferred Term	COVID-19
AE Onset Date / Rx Day	[redacted]20[redacted] / 122
Age at AE Onset	5[redacted]