M15-554 試験（投与 24 週時）

治験の標題： 1 種類以上の生物学的疾患修飾性抗リウマチ薬（bDMARD）による治療で効果不十分な活動性乾癬性関節炎患者におけるウパダシチニブ（ABT-494）とプラセボとの第 III 相ランダム化二重盲検比較試験-*SELECT-PsA2*	
治験実施施設： 16 ヵ国（ベルギー，ブラジル，カナダ，チリ，チェコ共和国，フランス，ギリシャ，ハンガリー，イタリア，日本，オランダ，ニュージーランド，ポルトガル，スペイン，イギリス，米国［プエルトリコを含む］），123 施設	
治験責任医師： [redacted], MD，他	
公表文献（参考資料）： なし	
治験期間（年数）： 最初の被験者の初回来院日：2017 年 5 月 [redacted] 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日（投与 24 週時）	開発のフェーズ：III
目的： 第 1 ピリオド 1. 生物学的疾患修飾性抗リウマチ薬（以下「bDMARD」）で効果不十分又は忍容性のない（以下「bDMARD-IR」）中等症から重症の活動性乾癬性関節炎患者を対象に，ウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）を投与したときの有効性（症状・徴候）をプラセボと比較する。 2. bDMARD-IR の中等症から重症の活動性乾癬性関節炎患者を対象に，ウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）を投与したときの安全性及び忍容性をプラセボと比較する。 第 2 ピリオド 第 1 ピリオドを完了した乾癬性関節炎患者を対象に，ウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）を投与したときの長期的な安全性，忍容性及び有効性を評価する。 本項には，第 1 ピリオドの投与 24 週時までの有効性データ，投与 24 週時までの短期的な安全性データ，及び 24 週間治験総括報告書（以下「CSR 24W」）の 20[redacted] 年 [redacted] 月 [redacted] 日のデータカットオフ日時点までの長期的な安全性データを含めた。	
被験者数（計画時と解析時）： 計画時：630 名，解析時：642 名（ウパダシチニブ 15 mg 群：211 名，30 mg 群：219 名，プラセボ群：212 名）	
診断と主要な組入れ基準： スクリーニング来院時の 6 ヵ月以上前に発症し，乾癬性関節炎の分類基準に基づき乾癬性関節炎と診断された 18 歳以上の成人男性及び女性を組み入れた。 以下の全てに該当する患者を適格な被験者とした： ● ベースライン時の疾患活動性を有する（スクリーニング及びベースライン来院時の圧痛関節数が 3 ヵ所以上［68 関節に基づく］及び腫脹関節数が 3 ヵ所以上［66 関節に基づく］と定義） ● 活動性尋常性乾癬と診断された又は尋常性乾癬の既往歴が確認できる ● 1 種類以上の bDMARD による治療で効果不十分（最低 12 週間の治療で効果が認められない）又は忍容性がない ● 治験薬初回投与前にすべての bDMARD の投与を中止している	

以下の患者を除外した：

- ヤヌスキナーゼ阻害薬（ルキソリチニブ，トファシチニブ，バリシチニブ及びフィルゴチニブを含むがこれらに限定しない）による治療歴がある
- ベースライン時に 3 種類以上の非生物学的疾患修飾性抗リウマチ薬（non-bDMARD）を投与している，メトトレキサート，スルファサラジン，レフルノミド，アプレミラスト，ヒドロキシクロロキン，ブシラミン若しくはイグラチモド以外の疾患修飾性抗リウマチ薬（以下「DMARD」）を使用している，又はメトトレキサートとレフルノミドを併用している
- 治験薬投与開始前の 30 日間又は薬剤の 5 半減期（どちらか長い方の期間）以内に，他の治験薬を使用した，又は登録時に他の介入臨床試験に組み入れられている
- 線維筋痛症の既往歴がある，17 歳以前に発現した関節炎の既往歴がある，又は乾癬性関節炎以外の炎症性関節疾患（関節リウマチ，痛風，結合組織疾患の合併，強皮症，多発性筋炎，皮膚筋炎，全身性エリテマトーデスを含むがこれらに限定しない）と診断されている（反応性関節炎又は軸性脊椎関節炎［強直性脊椎炎及び X 線検査で異常が認められない軸性脊椎関節炎を含む］の既往歴がある患者は，診断名が乾癬性関節炎に変更された，又は乾癬性関節炎の診断が追加された場合に組み入れ可能とした）
- スクリーニング期間中の臨床検査値が以下の基準に該当する：血清アスパラギン酸アミノトランスフェラーゼ（以下「AST」）が基準値上限（以下「ULN」）の 2 倍超，血清アラニンアミノトランスフェラーゼ（以下「ALT」）が ULN の 2 倍超，推定糸球体濾過率（4 変数を用いた Modification of Diet in Renal Disease 簡易式に基づく）が 40 mL/min/1.73m^2 未満，総白血球数が 2500/μL 未満，好中球数（絶対値）が 1500/μL 未満，血小板数が 100000/μL 未満，リンパ球数（絶対値）が 800/μL 未満，及びヘモグロビンが 10 g/dL 未満

治験方法：

本試験は国際共同第 III 相試験であり，倫理的配慮から過度な人数の被験者を組み入れることなく，科学的及び規制上の目的を達成するために，全世界の約 165 施設で約 630 名の被験者を組み入れる計画とした。

本試験は，2 つの投与期間で構成された。試験期間は以下のとおり構成することとした：1）35 日間のスクリーニング期間，2）24 週間のランダム化，二重盲検，並行群間，プラセボ対照投与期間，及びその後の追加 32 週間のウパダシチニブの用量を盲検とした投与期間からなる計 56 週間の盲検期間（第 1 ピリオド），3）投与期間の合計を約 3 年までとする長期継続投与期間（［最後の被験者が第 1 ピリオドの最終来院を完了するまで盲検とする］第 2 ピリオド），4）30 日間の電話連絡又は来院による追跡調査期間。

適格性基準を満たす被験者を乾癬の程度（体表面積［以下「BSA」］3%以上，3%未満），1 種類以上の DMARD の現在の使用の有無，及びこれまでに治療が奏効しなかった（効果不十分であった）bDMARD の数（1 又は 2 以上）によって層別化（但し，日本人被験者は乾癬の程度［BSA 3%以上，3%未満］のみにより層別化）し，2:2:1:1 の割合で 4 つの投与群のうち 1 つにランダム化することとした。

グループ 1：ウパダシチニブ 15 mg 1 日 1 回（N = 210）

グループ 2：ウパダシチニブ 30 mg 1 日 1 回（N = 210）

グループ 3：プラセボ→ウパダシチニブ 15 mg 1 日 1 回（N = 105）

グループ 4：プラセボ→ウパダシチニブ 30 mg 1 日 1 回（N = 105）

乾癬の程度が BSA の 3%未満の被験者は約 40%，2 種類以上の bDMARD が奏効しなかった被験者は約 30%をそれぞれ超えないように組入れを行うこととした。

被験薬，用量 / 含量 / 濃度，投与法，ロット番号：

ウパダシチニブ 15 mg 徐放錠（経口），バルクロット番号：[redacted]

ウパダシチニブ 30 mg 徐放錠（経口），バルクロット番号：[redacted]

治療期間：第 1 ピリオド：56 週間，第 2 ピリオド：最長 3 年間

対照薬，用量 / 含量 / 濃度，投与法，ロット番号：

ウパダシチニブに対応するプラセボの錠剤（経口），バルクロット番号：[redacted]，[redacted]
評価基準： 有効性： 主要評価項目は，投与 12 週時の米国リウマチ学会（以下「ACR」）20%改善基準を達成した被験者の割合（以下「ACR20 反応率」）とした。 主な多重性を調整した副次評価項目（特に記載がない限り，ウパダシチニブ各用量とプラセボの比較）： ● 投与 12 週時の健康評価質問票－障害指数（以下「HAQ-DI」）のベースラインからの変化量 ● 投与 16 週時において，乾癬の医師による静的全般的評価（以下「sIGA」）スコアが 0 又は 1 であり，ベースラインと比較して 2 ポイント以上の改善が認められた被験者の割合 ● 投与 16 週時の乾癬の面積と重症度の指数（以下「PASI」）75%改善基準を達成した被験者の割合（以下「PASI75 反応率」）（ベースラインで BSA の 3%以上の乾癬を有していた被験者が対象） ● 投与 12 週時の Short Form 36 項目健康調査票（以下「SF-36」）のベースラインからの変化量 ● 投与 12 週時の慢性疾患療法の機能的評価-倦怠感（以下「FACIT-F」）におけるベースラインからの変化量 ● 投与 24 週時の最低疾患活動性（以下「MDA」）を達成した被験者の割合 ● 投与 16 週時の乾癬症状自己評価（以下「SAPS」）質問票におけるベースラインからの変化量 追加の主な副次評価項目として，投与 12 週時の ACR50%改善基準を達成した被験者の割合（ACR50 反応率）及び ACR70%改善基準を達成した被験者の割合（以下「ACR70 反応率」），並びに投与 2 週時の ACR20 反応率を評価した。 追加の有効性評価項目として，治験実施計画書で規定した時点で以下の評価項目を評価した： ● ACR コアセットの各項目におけるベースラインからの変化量 ● ACR20/50/70 反応率 ● リーズ指趾炎指標（以下「LDI」）のベースラインからの変化量 ● 指趾炎数のベースラインからの変化量 ● 指趾炎が消失した被験者の割合 ● リーズ腱付着部炎指標（以下「LEI」）のベースラインからの変化量 ● 腱付着部炎が消失した被験者（LEI = 0）の割合 ● カナダ脊椎関節炎研究コンソーシアム（以下「SPARCC」）腱付着部炎指標のベースラインからの変化量 ● 腱付着部炎が消失した被験者（SPARCC 腱付着部炎指標= 0）の割合 ● 腱付着部炎総数のベースラインからの変化量 ● 腱付着部炎が消失した被験者（腱付着部炎総数= 0）の割合 ● PASI 75/90/100 反応率（ベースラインで BSA の 3%以上の乾癬を有していた被験者が対象） ● sIGA スコアの 0 又は 1 を達成し，ベースラインと比較して 2 ポイント以上の改善が認められた被験者の割合 ● 体表面積－乾癬（BSA-Ps）のベースラインからの変化量 ● 改変乾癬性関節炎反応基準（PsARC）に基づく奏効率 ● 28 関節に基づく疾患活動性スコア（以下「DAS28」）（C-反応性蛋白［CRP］）のベースラインからの変化量 ● DAS28（赤血球沈降速度［ESR］）のベースラインからの変化量 ● 乾癬性関節炎疾患活動性スコア（PASDAS）のベースラインからの変化量 ● 乾癬性関節炎疾患活動性（DAPSA）スコアのベースラインからの変化量 ● SF-36 身体的構成要素スコアのベースラインからの変化量 ● FACIT-F 質問票におけるベースラインからの変化量

- EuroQol 5 Dimensions 5 Levels（EQ-5D-5L）質問票におけるベースラインからの変化量
- 仕事の生産性及び活動障害（WPAI）質問票のベースラインからの変化量
- 健康資源活用（HRU）の累積数
- MDA を達成した被験者の割合
- SAPS 質問票におけるベースラインからの変化量
- 朝のこわばり（バース強直性脊椎炎疾患活動性指標［以下「BASDAI」］質問 5 及び 6 の平均値）のベースラインからの変化量
- 朝のこわばりの重症度及び期間のベースラインからの変化量
- HAQ-DI で臨床的意義のある改善（0.35 以上）を認めた被験者の割合
- BASDAI のベースラインからの変化量（ベースラインに乾癬性脊椎炎を有していた被験者が対象）
- BASDAI 50%改善（BASDAI50）反応率（ベースラインに乾癬性脊椎炎を有していた被験者が対象）
- 強直性脊椎炎疾患活動性スコア（以下「ASDAS」）のベースラインからの変化量（ベースラインに乾癬性脊椎炎を有していた被験者が対象）
- ASDAS における非活動性疾患を有する被験者の割合（ベースラインに乾癬性脊椎炎を有していた被験者が対象）
- ASDAS における主要改善を示した被験者の割合（ベースラインに乾癬性脊椎炎を有していた被験者が対象）
- ASDAS における臨床的に意義がある改善を示した被験者の割合（ベースラインに乾癬性脊椎炎を有していた被験者が対象）

薬物動態：
ウパダシチニブの血漿中濃度は，治験実施計画書で規定した時点に測定した。

安全性：
有害事象，バイタルサイン，身体検査及び臨床検査（血液学的検査，血液生化学検査及び尿検査）

統計手法：
有効性：
主要評価項目：解析は最大の解析対象集団を対象として，ランダム化された投与群に基づいて実施した。主要解析には，ノンレスポンダーインピュテーション（以下「NRI」）を用いた。ランダム化された各投与群について，点推定値及び正規近似に基づく 95%信頼区間を算出した。層別化因子である DMARD の現在の使用の有無で調整した Cochran Mantel Haenszel（以下「CMH」）検定を用いて，主要評価項目についてウパダシチニブ各用量群と併合したプラセボ群を比較した。点推定値，正規近似に基づく 95%信頼区間及び投与群の比較に関する *P* 値を示した。名目 *P* 値及び調整 *P* 値を示した。補足的な解析として，補完をせず，as observed（以下「AO」）データを用いて主要解析と同じ解析を実施した。missing not at random（以下「MNAR」）を含む，欠測値に関する様々な仮定について検討するため，ロジスティック回帰による多重補完により，ウパダシチニブ群とプラセボ群のそれぞれで ACR 反応率を体系的に 0%から 100%まで変化させて補完することにより，tipping point analysis を実施した。また，補足的な解析として，治験実施計画書に適合した解析対象集団を対象に NRI を用いた CMH 解析も実施した。
主な副次評価項目：2 値変数について，各投与群の頻度とパーセンテージ（%）を示した。主要解析として，有効性の評価の定義を除き，主要評価項目と同様の解析を実施した。部分集団のみに適用される評価項目については，部分集団のみを対象に同じ解析を実施した。投与 24 週時の MDA については，NRI を用いることに加え，救済療法基準に該当する被験者をノンレスポンダーとして取り扱った。ランダム化され，治験薬を 1 回以上投与された被験者を対象として，ウパダシチニブ各用量群とプラセボ群を比較した。補足的な解析として，2 値変数についても，AO データを用いて解析を実施した。ランダム化された各投与群について，点推定値及び正規近似に基づく 95%信頼区間を算出した。層別化因子である DMARD の現在の使用の有無で調整した CMH 検定を用いて，ウパダシチニブ各用量群と併合したプラセボ群を比較した。点推定値，正規近似に基づく 95%信頼区間及び

投与群間差に関する *P* 値を示した。

連続変数について，主要解析として，治療，来院，治療と来院の交互作用及び層別化因子である DMARD の現在の使用の有無を固定効果とし，ベースライン測定値を連続的固定共変量とする混合効果・反復測定モデルを用いて解析した。補足的な解析として，連続変数の順位付けした副次評価項目について，AO データを用い，また，投与群及び層別化因子である DMARD の現在の使用の有無を固定効果とし，対応するベースライン測定値を共変量とする共分散分析（以下「ANCOVA」）を用いて解析した。ランダム化された各投与群の最小二乗平均値及び 95%信頼区間，並びにウパダシチニブ各用量群と併合したプラセボ群間の投与群間差の最小二乗平均値，その 95%信頼区間及び *P* 値を示した。順位付けした主な副次評価項目について，調整 *P* 値を示した。

追加の有効性評価項目については，主な副次評価項目と同じ解析を実施した。

薬物動態：

各来院時の被験者別のウパダシチニブ血漿中濃度を一覧表にし，適切な統計手法を用いて要約した。非線形混合効果モデルを用いた解析により，ウパダシチニブの見かけのクリアランス及び分布容積の母集団中心値及び経験的ベイズ推定法による個別値を推定した。

安全性：

投与 24 週時までの安全性解析及び長期安全性解析（20[redacted] 年 [redacted] 月 [redacted] 日の CSR 24W のデータカットオフ日まで）の 2 つの解析を行うこととした。

投与 24 週時まで：標準的な安全性解析として，有害事象，臨床検査値及びバイタルサインを評価した。各投与群の有害事象を発現した被験者数及び発現割合の表を，ICH 国際医薬用語集（以下「MedDRA」）の器官別大分類別及び基本語別に示した。各来院日の臨床検査値及びバイタルサインの連続変数は投与群別に要約した。臨床的に意義がある臨床検査値及びバイタルサインの基準に該当した被験者の集計表を投与群別に示した。安全性データの欠測値は補完しなかった。ウパダシチニブ群とプラセボ群の比較は，主な安全性評価項目である有害事象の概要，特に注目すべき有害事象の概要，特定の臨床検査パラメータのベースラインからの変化量及び臨床的に意義がある臨床検査値について示した。投与群間差及びその 95%信頼区間を示した。投与 24 週時までは，治験実施計画書に規定した治療切替えは起こらなかった。

治験実施計画書に規定した治療切替えを考慮した長期安全性解析として，累積曝露量で調整した有害事象の発現件数，来院日別の臨床検査値及びバイタルサインの要約，並びに臨床的に意義がある臨床検査値及びバイタルサインの発現割合を評価した。100 人年あたりの有害事象の発現件数は，有害事象が発現した時点の実際に受けた投与に基づく投与群別に示した。有害事象が発現した被験者の一覧を器官別大分類及び基本語別に示した。来院日別の臨床検査値及びバイタルサインの要約は実際に受けた投与に基づく投与群の順序別に示した。臨床的に意義がある臨床検査値及びバイタルサインの基準に該当した被験者の集計表及び一覧を事象が発現した時点の実際に受けた投与に基づく投与群別に示した。安全性データの欠測値は補完しなかった。

実際に受けた投与に基づく投与群の順序は以下のとおり定義した。

1. プラセボ→ウパダシチニブ 15 mg 1 日 1 回
2. プラセボ→ウパダシチニブ 30 mg 1 日 1 回
3. ウパダシチニブ 15 mg 1 日 1 回
4. ウパダシチニブ 30 mg 1 日 1 回

要約 / 結論：

有効性の結果：

本 24 週間の二重盲検，プラセボ対照投与期間の解析において，bDMARD-IR の中等症から重症の活動性乾癬性関節炎患者に対するウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）の投与の有効性が示された。ウパダシチニブ 15 mg 群及び 30 mg 群のいずれにおいてもプラセボ群と比較して主要評価項目及び全ての順位付けした副次評価項目において統計学的に有意な改善が認められた。順位付けしない副次評価項目においても一貫した結果が得られことからも，有効性が支持された。

主要評価項目では，投与 12 週時の ACR20 反応率は，ウパダシチニブ 15 mg 群及び 30 mg 群のいずれにおいても

プラセボ群と比較して統計学的に有意に高く，ウパダシチニブが乾癬性関節炎の関節炎症状の治療に有効であることが示された。ACR20/50 反応率は，投与 2 週時にはウパダシチニブ群においてプラセボ群と比較して高くなり，効果は投与 24 週時まで継続した。ACR70 反応率は，投与 4 週時から認められ，効果は投与 24 週時まで継続した。

乾癬性関節炎の疾患活動性の包括的評価指標の全てについて，ウパダシチニブ 15 mg 群及び 30 mg 群においてプラセボ群と比較して統計学的に有意な改善が認められ，ほとんどで名目 *P* 値< 0.05 であった。乾癬性関節炎の疾患活動性の包括的評価指標の平均値は，投与 12 週時から投与 24 週時まで維持又は更に改善した。

ベースラインに乾癬性脊椎炎を有していた被験者において，BASDAI 及び ASDAS スコアは，ウパダシチニブ 15 mg 群及び 30 mg 群においてプラセボ群と比較して，投与 12 週時に改善し（名目 *P* 値< 0.05），投与 24 週時に更に改善した。

また，ウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）の投与により，乾癬の症状・徴候が改善し，腱付着部炎，指趾炎及び朝のこわばりが改善又は消失し，並びに健康関連生活の質，身体機能及び倦怠感が改善した。

薬物動態の結果：

投与後 24 時間以内でのウパダシチニブの平均血漿中濃度は，15 mg（1 日 1 回）では 5.8～32.1 ng/mL，30 mg（1 日 1 回）では 13.2～50.9 ng/mL であった。ウパダシチニブの濃度の実測値は，既存の薬物動態の結果から予測される濃度と一致した。

安全性の結果：

ウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）の投与は，CSR 24W のデータカットオフ日まで，おおむね安全であり，忍容性は良好であった。本試験でのウパダシチニブの観察された安全性プロファイルは，関節リウマチ試験で観察されたものとおおむね一致していた。新規の安全性リスクは確認されなかった。主な安全性データの要約を下記に示した：

- 重篤な有害事象，高度の有害事象，及び治験薬の投与中止に至った有害事象の発現割合は，プラセボ群と比較してウパダシチニブ群で高かった。データカットオフまで，重篤な有害事象及び治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，ウパダシチニブ 15 mg 群及び 30 mg 群で同程度であった。
- 多く認められた有害事象（ウパダシチニブ 15 mg 群又は 30 mg 群で 5%以上の被験者に発現）は，上気道感染，上咽頭炎，気管支炎，尿路感染，インフルエンザ，下痢，悪心及び血中クレアチンホスホキナーゼ増加であった。
- 有害事象発現件数は大部分の注目すべき有害事象で少なく，これらの有害事象の発現割合はプラセボ群とウパダシチニブ 15 mg 群でおおむね同程度であった。データカットオフまで，重篤な感染症，日和見感染，帯状疱疹，肝障害，貧血，好中球減少症及びクレアチンホスホキナーゼ（以下「CPK」）増加の 100 人年あたりの発現件数は，ウパダシチニブ 15 mg 群と比較して 30 mg 群で高かった。
- 帯状疱疹の多くは，非播種性（皮膚分節が 1～2 箇所に限定），重症度は軽度又は中等度であり，治験薬の投与中止には至らなかった。
- 肝障害の多くは ALT 又は AST 増加であり，重篤なものはなく，重症度はほとんどが軽度又は中等度であった。治験薬の投与中止に至った事象はほとんどなかった。グレード 3 又はグレード 4 の ALT 又は AST 増加の発現は少なかった。グレード 3 の血液生化学検査値の上昇の多くは一時的であり，再検査では確認されなかった。Hy's law に該当する被験者はいなかった。
- 貧血，好中球減少症，及びリンパ球減少症の多くは，重症度が軽度又は中等度であり，少数に認められたグレード 3 の血液学的検査値の減少は一時的であり，再検査では確認されなかった。グレード 4 のヘモグロビン，好中球数，リンパ球数の減少はなかった。
- グレード 3 及びグレード 4 の CPK 増加は少なく，発現は単発的であった。すべての CPK 増加の事象は，非重篤，重症度は軽度又は中等度であり，治験薬の投与中止に至ったものはなく，横紋筋融解症の事象は報告されなかった。ウイルス性筋炎の事象がウパダシチニブ 15 mg 群の 1 名に報告された。その

他には筋炎の事象は報告されなかった。

- 悪性腫瘍の発現割合は，ウパダシチニブ 15 mg 群及び 30 mg 群において同程度であった。リンパ球形態異常がウパダシチニブ 15 mg 群の 2 名に報告され，MedDRA 標準検索式の「悪性リンパ腫」に該当した。いずれも，リンパ腫の確定診断は受けなかった。
- 主要心血管イベントと判定された事象が，ウパダシチニブ 15 mg 群と 30 mg 群にそれぞれ 1 件報告された。コレステロール，高比重リポ蛋白コレステロール（以下「HDL-C」）及び低比重リポ蛋白コレステロール（以下「LDL-C」）の増加がウパダシチニブ投与で認められた。LDL-C/HDL-C 比及び総コレステロール/HDL-C 比にベースラインから本質的な変化はなかった。静脈血栓塞栓症と判定された事象がウパダシチニブ 15 mg 群に 1 件報告された。
- プラセボ群で 1 名が交通事故により死亡した。ウパダシチニブ 30 mg 群で 1 名が死亡し，死因は，死亡診断書では急性呼吸窮迫症候群及び右側気胸と記載されたが，治験責任医師は，複雑な臨床経過後の汎血球減少症及び複数の合併する病状によるものと判断した。
- 活動性結核又は消化管穿孔と判定された事象は，いずれの投与群でも報告されなかった。
- ウパダシチニブを投与された被験者の体重増加を除き，バイタイルサインに重要な変化は認められなかった。

結論：

本試験（M15-554 試験）の投与 24 週時（第 1 ピリオド）までの解析において，有効性では，bDMARD-IR の中等症から重症の活動性乾癬性関節炎患者における臨床的反応及び患者報告健康アウトカムのいずれについても，プラセボと比較してウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）で優れた結果が示された。安全性では，ウパダシチニブ 15 mg 及び 30 mg の忍容性はおおむね良好であることが確認された。本試験の投与 24 週までの有効性の結果及び CSR 24W のデータカットオフ日までの安全性の結果より，ウパダシチニブ 15 mg 及び 30 mg のベネフィット・リスクのプロファイルは良好と考えられた。

表 1. 投与 24 週時までの有害事象を発現した被験者数及び発現割合：MedDRA のプライマリー器官別大分類及び基本語別（安全性解析対象集団）

相互参照：M15-554 試験 CSR W24 Table 14.3__1.2.1

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
Any adverse event	139 (65.6)	135 (64.0)	170 (78.0)
血液およびリンパ系障害	3 (1.4)	7 (3.3)	16 (7.3)
貧血	1 (0.5)	1 (0.5)	10 (4.6)
失血性貧血	0	1 (0.5)	0
内出血発生の増加傾向	0	1 (0.5)	0
鉄欠乏性貧血	0	1 (0.5)	1 (0.5)
白血球減少症	0	0	2 (0.9)
リンパ球増加症	0	0	1 (0.5)
リンパ球減少症	0	0	2 (0.9)
好中球減少症	1 (0.5)	2 (0.9)	2 (0.9)
好中球増加症	0	1 (0.5)	0
血小板減少症	1 (0.5)	0	1 (0.5)
血小板増加症	0	0	1 (0.5)
心臓障害	2 (0.9)	9 (4.3)	6 (2.8)
急性心筋梗塞	0	1 (0.5)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
心臓障害 (Cont.)			
不安定狭心症	1 (0.5)	0	1 (0.5)
心房細動	0	1 (0.5)	1 (0.5)
徐脈	0	1 (0.5)	1 (0.5)
うっ血性心不全	1 (0.5)	0	0
心肺停止	0	1 (0.5)	0
冠動脈狭窄	0	0	1 (0.5)
僧帽弁閉鎖不全症	1 (0.5)	0	0
動悸	0	4 (1.9)	0
洞性徐脈	0	0	1 (0.5)
洞性頻脈	0	0	1 (0.5)
頻脈	0	1 (0.5)	0
心室細動	0	1 (0.5)	0
先天性、家族性および遺伝性障害	1 (0.5)	0	1 (0.5)
陰嚢水瘤	0	0	1 (0.5)
ミトコンドリアミオパチー	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
耳および迷路障害	0	1 (0.5)	3 (1.4)
耳不快感	0	0	1 (0.5)
回転性めまい	0	1 (0.5)	2 (0.9)
内分泌障害	1 (0.5)	1 (0.5)	3 (1.4)
自己免疫性甲状腺炎	0	0	1 (0.5)
甲状腺腫	1 (0.5)	0	0
甲状腺機能亢進症	0	0	1 (0.5)
甲状腺機能低下症	0	1 (0.5)	2 (0.9)
甲状腺腫瘤	0	0	1 (0.5)
眼障害	3 (1.4)	4 (1.9)	6 (2.8)
一過性黒内障	0	0	1 (0.5)
眼瞼炎	0	0	1 (0.5)
白内障	1 (0.5)	1 (0.5)	0
霰粒腫	0	1 (0.5)	1 (0.5)
眼痛	0	0	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
眼障害 (Cont.)			
眼そう痒症	1 (0.5)	0	0
緑内障	0	0	1 (0.5)
眼部不快感	0	0	1 (0.5)
後嚢部混濁	0	1 (0.5)	0
ぶどう膜炎	1 (0.5)	0	0
霧視	0	1 (0.5)	0
胃腸障害	31 (14.6)	38 (18.0)	39 (17.9)
腹部不快感	1 (0.5)	2 (0.9)	0
腹部膨満	0	1 (0.5)	0
腹痛	1 (0.5)	3 (1.4)	3 (1.4)
上腹部痛	3 (1.4)	2 (0.9)	3 (1.4)
アフタ性潰瘍	0	0	1 (0.5)
バレット食道	0	1 (0.5)	0
大腸炎	0	0	1 (0.5)
便秘	1 (0.5)	3 (1.4)	5 (2.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
胃腸障害 (Cont.)			
クローン病	1 (0.5)	0	0
齲歯	0	1 (0.5)	0
下痢	12 (5.7)	5 (2.4)	12 (5.5)
口内乾燥	2 (0.9)	2 (0.9)	2 (0.9)
消化不良	0	2 (0.9)	3 (1.4)
嚥下障害	0	0	1 (0.5)
びらん性食道炎	1 (0.5)	0	0
鼓腸	2 (0.9)	0	0
食中毒	0	1 (0.5)	1 (0.5)
胃出血	0	0	1 (0.5)
胃炎	1 (0.5)	1 (0.5)	1 (0.5)
びらん性胃炎	0	1 (0.5)	0
胃腸障害	1 (0.5)	0	0
胃食道逆流性疾患	2 (0.9)	2 (0.9)	0
歯肉障害	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
胃腸障害 (Cont.)			
歯肉退縮	0	1 (0.5)	0
痔出血	0	1 (0.5)	0
痔核	0	3 (1.4)	1 (0.5)
過敏性腸症候群	2 (0.9)	0	0
大腸ポリープ	1 (0.5)	0	0
腰ヘルニア	0	1 (0.5)	0
口腔内潰瘍形成	0	2 (0.9)	2 (0.9)
悪心	7 (3.3)	4 (1.9)	11 (5.0)
消化性潰瘍	1 (0.5)	0	0
直腸出血	0	0	1 (0.5)
直腸潰瘍	0	1 (0.5)	0
小腸出血	0	0	1 (0.5)
小腸潰瘍	0	0	1 (0.5)
口内炎	2 (0.9)	1 (0.5)	2 (0.9)
舌腫脹	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
胃腸障害 (Cont.)			
歯の脱落	1 (0.5)	0	0
歯痛	0	0	1 (0.5)
臍ヘルニア	0	1 (0.5)	0
嘔吐	5 (2.4)	0	4 (1.8)
一般・全身障害および投与部位の状態	12 (5.7)	8 (3.8)	17 (7.8)
無力症	2 (0.9)	0	0
胸部不快感	0	0	1 (0.5)
胸痛	1 (0.5)	1 (0.5)	0
悪寒	0	0	1 (0.5)
薬物不耐性	1 (0.5)	1 (0.5)	2 (0.9)
疲労	1 (0.5)	2 (0.9)	3 (1.4)
インフルエンザ様疾患	0	0	1 (0.5)
注射部位発疹	1 (0.5)	0	0
倦怠感	1 (0.5)	0	0
非心臓性胸痛	0	0	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
浮腫	1 (0.5)	0	0
末梢性浮腫	0	2 (0.9)	2 (0.9)
疼痛	1 (0.5)	0	0
末梢腫脹	2 (0.9)	0	1 (0.5)
発熱	0	3 (1.4)	4 (1.8)
全身性炎症反応症候群	0	0	1 (0.5)
圧痛	1 (0.5)	0	0
肝胆道系障害	1 (0.5)	0	6 (2.8)
胆石症	0	0	2 (0.9)
胆嚢ポリープ	0	0	1 (0.5)
肝嚢胞	0	0	1 (0.5)
脂肪肝	1 (0.5)	0	0
過形成性胆嚢症	0	0	1 (0.5)
肝損傷	0	0	1 (0.5)

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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
免疫系障害	1 (0.5)	0	3 (1.4)
造影剤アレルギー	0	0	1 (0.5)
薬物過敏症	0	0	2 (0.9)
季節性アレルギー	1 (0.5)	0	1 (0.5)
感染症および寄生虫症	72 (34.0)	70 (33.2)	107 (49.1)
膿瘍	1 (0.5)	0	0
四肢膿瘍	0	0	2 (0.9)
急性副鼻腔炎	0	1 (0.5)	1 (0.5)
肛門カンジダ症	0	1 (0.5)	0
菌血症	0	0	1 (0.5)
細菌性膣症	0	2 (0.9)	0
細菌尿	0	0	1 (0.5)
気管支炎	5 (2.4)	10 (4.7)	12 (5.5)
ブドウ球菌感染性滑液包炎	1 (0.5)	0	0
カンジダ感染	0	0	1 (0.5)
気管カンジダ症	0	0	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
感染症および寄生虫症 (Cont.)			
蜂巣炎	0	2 (0.9)	3 (1.4)
眼窩蜂巣炎	1 (0.5)	0	0
結膜炎	1 (0.5)	0	0
ウイルス性結膜炎	0	1 (0.5)	0
膀胱炎	1 (0.5)	2 (0.9)	1 (0.5)
毛嚢虫症	0	0	1 (0.5)
憩室炎	0	0	1 (0.5)
耳感染	4 (1.9)	0	1 (0.5)
エンテロウイルス感染	0	0	1 (0.5)
精巣上体炎	0	0	1 (0.5)
大腸菌性尿路感染	1 (0.5)	0	0
硬膜外膿瘍	0	0	1 (0.5)
眼感染	0	0	1 (0.5)
毛包炎	1 (0.5)	3 (1.4)	2 (0.9)
真菌感染	0	1 (0.5)	0

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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
感染症および寄生虫症 (Cont.)			
皮膚真菌感染	0	0	2 (0.9)
せつ	1 (0.5)	0	0
胃腸炎	2 (0.9)	3 (1.4)	6 (2.8)
ウイルス性胃腸炎	1 (0.5)	3 (1.4)	1 (0.5)
陰部ヘルペス	0	1 (0.5)	1 (0.5)
肛径部膿瘍	1 (0.5)	0	0
単純ヘルペス	0	1 (0.5)	1 (0.5)
帯状疱疹	2 (0.9)	3 (1.4)	8 (3.7)
麦粒腫	2 (0.9)	0	1 (0.5)
感染性皮膚嚢腫	1 (0.5)	0	0
インフルエンザ	3 (1.4)	8 (3.8)	11 (5.0)
腎感染	0	0	1 (0.5)
肺感染	1 (0.5)	0	0
爪感染	1 (0.5)	1 (0.5)	0
上咽頭炎	17 (8.0)	10 (4.7)	20 (9.2)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
感染症および寄生虫症 (Cont.)			
口腔カンジダ症	0	1 (0.5)	4 (1.8)
口腔ヘルペス	2 (0.9)	0	3 (1.4)
中咽頭カンジダ症	0	0	1 (0.5)
中耳炎	1 (0.5)	0	2 (0.9)
歯周炎	1 (0.5)	0	0
咽頭炎	1 (0.5)	2 (0.9)	2 (0.9)
レンサ球菌性咽頭炎	0	3 (1.4)	2 (0.9)
肺炎	2 (0.9)	1 (0.5)	3 (1.4)
膿尿	0	0	1 (0.5)
気道感染	2 (0.9)	0	3 (1.4)
ウイルス性気道感染	1 (0.5)	0	0
鼻炎	0	1 (0.5)	0
副鼻腔炎	9 (4.2)	5 (2.4)	6 (2.8)
細菌性副鼻腔炎	2 (0.9)	0	0
皮膚カンジダ	0	0	1 (0.5)

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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
感染症および寄生虫症 (Cont.)			
足部白癬	0	2 (0.9)	2 (0.9)
癜風	1 (0.5)	0	0
扁桃炎	1 (0.5)	0	1 (0.5)
歯膿瘍	0	1 (0.5)	0
歯感染	1 (0.5)	1 (0.5)	1 (0.5)
気管炎	2 (0.9)	0	0
気管気管支炎	0	0	1 (0.5)
上気道感染	10 (4.7)	13 (6.2)	23 (10.6)
尿路感染	12 (5.7)	9 (4.3)	11 (5.0)
腸球菌性尿路感染	0	1 (0.5)	0
ウイルス感染	0	0	1 (0.5)
ウイルス性筋炎	0	1 (0.5)	0
ウイルス性発疹	0	0	1 (0.5)
ウイルス性扁桃炎	0	1 (0.5)	0
ウイルス性上気道感染	1 (0.5)	2 (0.9)	3 (1.4)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
感染症および寄生虫症 (Cont.)			
外陰部腟カンジダ症	2 (0.9)	0	3 (1.4)
傷害、中毒および処置合併症	11 (5.2)	22 (10.4)	21 (9.6)
動物咬傷	1 (0.5)	1 (0.5)	1 (0.5)
足関節部骨折	1 (0.5)	1 (0.5)	0
剥離骨折	0	1 (0.5)	0
第2度熱傷	0	0	1 (0.5)
挫傷	0	3 (1.4)	4 (1.8)
角膜擦過傷	0	0	1 (0.5)
上顆炎	0	1 (0.5)	0
転倒	0	1 (0.5)	5 (2.3)
大腿骨頚部骨折	0	0	1 (0.5)
腓骨骨折	1 (0.5)	0	0
足骨折	0	2 (0.9)	0
凍傷	0	0	1 (0.5)
関節脱臼	0	1 (0.5)	0

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TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
傷害、中毒および処置合併症 (Cont.)			
関節損傷	0	2 (0.9)	1 (0.5)
靭帯捻挫	2 (0.9)	0	2 (0.9)
四肢損傷	0	3 (1.4)	1 (0.5)
つち指	0	1 (0.5)	0
筋損傷	0	0	1 (0.5)
肉離れ	0	1 (0.5)	0
膝蓋骨骨折	0	1 (0.5)	0
処置による疼痛	1 (0.5)	2 (0.9)	1 (0.5)
肋骨骨折	1 (0.5)	0	0
交通事故	2 (0.9)	0	0
皮膚擦過傷	0	0	1 (0.5)
皮膚裂傷	0	3 (1.4)	1 (0.5)
脊椎圧迫骨折	1 (0.5)	0	1 (0.5)
ストレス骨折	0	0	1 (0.5)
熱傷	0	0	1 (0.5)

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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
傷害、中毒および処置合併症 (Cont.)			
歯牙破折	1 (0.5)	1 (0.5)	2 (0.9)
各種物質毒性	1 (0.5)	0	0
外傷性関節炎	0	1 (0.5)	0
外傷性血胸	1 (0.5)	0	0
血管偽動脈瘤	1 (0.5)	0	0
臨床検査	12 (5.7)	17 (8.1)	36 (16.5)
アラニンアミノトランスフェラーゼ増加	1 (0.5)	2 (0.9)	8 (3.7)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.5)	0	7 (3.2)
血中アルカリホスファターゼ増加	0	0	1 (0.5)
血中ビリルビン増加	0	1 (0.5)	1 (0.5)
血中コレステロール増加	0	1 (0.5)	0
血中クレアチンホスホキナーゼMB増加	1 (0.5)	0	0
血中クレアチンホスホキナーゼ増加	4 (1.9)	4 (1.9)	12 (5.5)
血中クレアチニン増加	0	0	1 (0.5)
血中ブドウ糖増加	0	2 (0.9)	1 (0.5)

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TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
臨床検査 (Cont.)			
血中カリウム増加	0	1 (0.5)	0
血圧上昇	0	0	1 (0.5)
収縮期血圧上昇	0	0	1 (0.5)
血中テストステロン減少	0	1 (0.5)	1 (0.5)
血中トリグリセリド増加	0	0	1 (0.5)
血中尿素増加	0	0	1 (0.5)
血中尿酸増加	0	0	1 (0.5)
心雑音	0	0	1 (0.5)
ヘマトクリット減少	0	1 (0.5)	0
ヘモグロビン減少	1 (0.5)	1 (0.5)	3 (1.4)
肝酵素上昇	1 (0.5)	0	4 (1.8)
肝機能検査値上昇	0	0	1 (0.5)
リンパ球数減少	0	2 (0.9)	0
リンパ球数増加	0	0	1 (0.5)
リンパ球形態異常	0	1 (0.5)	0

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TABLE 14.3__1.2.1

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- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
臨床検査 (Cont.)			
骨髄球数増加	1 (0.5)	0	0
好中球数減少	0	0	5 (2.3)
好中球数増加	0	1 (0.5)	0
前立腺特異性抗原増加	1 (0.5)	0	0
赤血球数減少	0	1 (0.5)	0
トランスアミナーゼ上昇	0	1 (0.5)	1 (0.5)
尿中尿酸減少	1 (0.5)	0	0
超低比重リポ蛋白増加	0	0	1 (0.5)
体重減少	0	0	1 (0.5)
体重増加	2 (0.9)	1 (0.5)	2 (0.9)
白血球数減少	0	3 (1.4)	1 (0.5)
白血球数増加	0	1 (0.5)	0
代謝および栄養障害	9 (4.2)	14 (6.6)	12 (5.5)
食欲減退	0	0	1 (0.5)
糖尿病	1 (0.5)	2 (0.9)	0

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TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
代謝および栄養障害 (Cont.)			
脂質異常症	0	0	1 (0.5)
高カルシウム血症	0	0	1 (0.5)
高コレステロール血症	0	3 (1.4)	0
高血糖	1 (0.5)	1 (0.5)	1 (0.5)
高カリウム血症	1 (0.5)	1 (0.5)	0
高脂血症	1 (0.5)	5 (2.4)	1 (0.5)
高トリグリセリド血症	1 (0.5)	1 (0.5)	2 (0.9)
高尿酸血症	1 (0.5)	0	0
低血糖	0	0	2 (0.9)
低カリウム血症	1 (0.5)	1 (0.5)	0
低ナトリウム血症	0	1 (0.5)	0
インスリン抵抗性	1 (0.5)	0	0
2型糖尿病	2 (0.9)	0	0
ビタミンB12欠乏	0	0	2 (0.9)
ビタミンD欠乏	0	2 (0.9)	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
筋骨格系および結合組織障害	24 (11.3)	31 (14.7)	26 (11.9)
関節痛	3 (1.4)	3 (1.4)	3 (1.4)
背部痛	3 (1.4)	6 (2.8)	5 (2.3)
滑液包炎	0	3 (1.4)	2 (0.9)
尾骨痛	0	0	1 (0.5)
指炎	1 (0.5)	0	0
外骨腫	0	0	1 (0.5)
顎骨の外骨腫	0	0	1 (0.5)
椎間関節症候群	1 (0.5)	0	0
側腹部痛	1 (0.5)	1 (0.5)	0
椎間板変性症	1 (0.5)	0	0
椎間板障害	0	1 (0.5)	0
椎間板突出	1 (0.5)	0	1 (0.5)
関節腫脹	1 (0.5)	0	1 (0.5)
筋痙縮	2 (0.9)	2 (0.9)	3 (1.4)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
筋骨格系および結合組織障害 (Cont.)			
筋攣縮	1 (0.5)	0	0
筋骨格痛	1 (0.5)	0	0
筋肉痛	0	1 (0.5)	2 (0.9)
筋膜疼痛症候群	1 (0.5)	0	0
頚部痛	1 (0.5)	0	1 (0.5)
変形性関節症	0	1 (0.5)	1 (0.5)
骨壊死	0	1 (0.5)	0
四肢痛	0	0	2 (0.9)
関節周囲炎	1 (0.5)	0	0
足底筋膜炎	0	0	1 (0.5)
乾癬性関節症	11 (5.2)	10 (4.7)	3 (1.4)
急速進行性変形性関節症	0	1 (0.5)	0
肩回旋筋腱板症候群	0	0	2 (0.9)
変形性脊椎症	1 (0.5)	0	0
脊柱管狭窄症	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
筋骨格系および結合組織障害 (Cont.)			
脊椎すべり症	1 (0.5)	0	0
滑液嚢腫	0	2 (0.9)	0
全身性エリテマトーデス	0	1 (0.5)	0
腱炎	0	1 (0.5)	0
腱鞘炎	0	1 (0.5)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.9)	4 (1.9)	3 (1.4)
基底細胞癌	0	1 (0.5)	1 (0.5)
異形成母斑	1 (0.5)	0	0
子宮内膜癌	0	0	1 (0.5)
卵巣癌	0	0	1 (0.5)
前立腺癌	0	1 (0.5)	0
直腸腺癌	0	0	1 (0.5)
直腸癌	0	1 (0.5)	0
子宮平滑筋腫	1 (0.5)	1 (0.5)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
神経系障害	14 (6.6)	12 (5.7)	25 (11.5)
手根管症候群	0	1 (0.5)	2 (0.9)
糖尿病性ニューロパチー	0	0	1 (0.5)
浮動性めまい	2 (0.9)	4 (1.9)	6 (2.8)
頭部不快感	0	0	1 (0.5)
頭痛	6 (2.8)	4 (1.9)	9 (4.1)
筋緊張亢進	1 (0.5)	0	0
感覚鈍麻	0	1 (0.5)	0
腰髄神経根障害	1 (0.5)	0	0
腰仙部神経根障害	0	0	1 (0.5)
片頭痛	1 (0.5)	1 (0.5)	2 (0.9)
錯感覚	1 (0.5)	1 (0.5)	0
多発ニューロパチー	1 (0.5)	0	0
ヘルペス後神経痛	0	0	3 (1.4)
失神寸前の状態	0	0	1 (0.5)
会話障害	0	1 (0.5)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
神経系障害 (Cont.)			
失神	1 (0.5)	1 (0.5)	0
緊張性頭痛	0	0	1 (0.5)
一過性全健忘	0	0	1 (0.5)
振戦	0	1 (0.5)	0
妊娠、産褥および周産期の状態	0	0	1 (0.5)
異所性妊娠	0	0	1 (0.5)
精神障害	11 (5.2)	8 (3.8)	11 (5.0)
感情不安定	0	0	1 (0.5)
不安	5 (2.4)	2 (0.9)	1 (0.5)
うつ病	5 (2.4)	2 (0.9)	7 (3.2)
失見当識	0	1 (0.5)	0
薬物乱用	0	0	1 (0.5)
不眠症	1 (0.5)	2 (0.9)	0
リビドー減退	0	0	1 (0.5)
悪夢	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
精神障害 (Cont.)			
パニック発作	0	1 (0.5)	1 (0.5)
腎および尿路障害	3 (1.4)	6 (2.8)	5 (2.3)
急性腎障害	1 (0.5)	0	1 (0.5)
膀胱拡大	0	0	1 (0.5)
膀胱結石	0	0	1 (0.5)
着色尿	0	0	1 (0.5)
血尿	0	2 (0.9)	0
白血球尿	0	1 (0.5)	1 (0.5)
腎結石症	0	2 (0.9)	0
蛋白尿	1 (0.5)	1 (0.5)	0
腎仙痛	0	1 (0.5)	0
腎嚢胞	0	0	1 (0.5)
尿管結石症	1 (0.5)	0	0
生殖系および乳房障害	3 (1.4)	5 (2.4)	5 (2.3)
亀頭包皮炎	0	1 (0.5)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
生殖系および乳房障害 (Cont.)			
良性前立腺肥大症	0	0	2 (0.9)
乳房嚢胞	1 (0.5)	0	0
乳房腫瘤	0	0	1 (0.5)
勃起不全	0	0	1 (0.5)
月経過多	0	1 (0.5)	0
卵巣嚢胞	0	1 (0.5)	0
前立腺石灰化	0	0	1 (0.5)
前立腺炎	0	1 (0.5)	0
腟分泌物	1 (0.5)	0	0
腟異形成	0	1 (0.5)	0
腟出血	0	1 (0.5)	0
外陰腟そう痒症	1 (0.5)	0	0
外陰腟発疹	1 (0.5)	0	0
呼吸器、胸郭および縦隔障害	15 (7.1)	13 (6.2)	13 (6.0)
急性呼吸不全	0	1 (0.5)	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
喘息	1 (0.5)	0	2 (0.9)
気管支反応性亢進	0	1 (0.5)	0
慢性閉塞性肺疾患	0	0	2 (0.9)
咳嗽	5 (2.4)	5 (2.4)	7 (3.2)
呼吸困難	0	1 (0.5)	1 (0.5)
労作性呼吸困難	0	1 (0.5)	0
鼻出血	1 (0.5)	1 (0.5)	0
鼻閉	2 (0.9)	0	0
口腔咽頭痛	3 (1.4)	2 (0.9)	2 (0.9)
肺塞栓症	0	1 (0.5)	0
肺腫瘤	0	0	1 (0.5)
気道うっ血	0	2 (0.9)	1 (0.5)
アレルギー性鼻炎	2 (0.9)	0	0
鼻漏	1 (0.5)	0	0
副鼻腔うっ血	0	1 (0.5)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
声帯障害	1 (0.5)	0	0
皮膚および皮下組織障害	16 (7.5)	9 (4.3)	19 (8.7)
ざ瘡	1 (0.5)	3 (1.4)	4 (1.8)
脱毛症	1 (0.5)	0	3 (1.4)
水疱	0	0	1 (0.5)
皮膚炎	0	1 (0.5)	0
薬疹	0	0	1 (0.5)
斑状出血	1 (0.5)	0	3 (1.4)
多汗症	0	1 (0.5)	0
汗疹	0	1 (0.5)	1 (0.5)
寝汗	0	0	1 (0.5)
爪甲剥離症	1 (0.5)	0	0
光線過敏性反応	1 (0.5)	0	0
乾癬	8 (3.8)	1 (0.5)	1 (0.5)
発疹	3 (1.4)	0	4 (1.8)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.2.1

Subjects with Treatment-Emergent Adverse Events by Primary MedDRA System Organ Class and Preferred Term
- up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
皮膚および皮下組織障害 (Cont.)			
斑状皮疹	0	1 (0.5)	0
そう痒性皮疹	0	0	1 (0.5)
小水疱性皮疹	0	1 (0.5)	0
酒さ	0	0	1 (0.5)
皮膚病変	0	0	1 (0.5)
蕁麻疹	0	0	1 (0.5)
血管障害	11 (5.2)	4 (1.9)	5 (2.3)
高血圧	9 (4.2)	4 (1.9)	4 (1.8)
低血圧	1 (0.5)	0	1 (0.5)
レイノー現象	1 (0.5)	0	0
収縮期高血圧	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

表 2.　投与 24 週時までの治験薬と関連ありの有害事象を発現した被験者数及び発現割合：MedDRA のプライマリー器官別大分類及び基本語別（安全性解析対象集団）

相互参照：M15-554 試験 CSR W24 Table 14.3__1.6.1

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
Any adverse event	53 (25.0)	55 (26.1)	79 (36.2)
血液およびリンパ系障害	0	4 (1.9)	10 (4.6)
貧血	0	1 (0.5)	5 (2.3)
失血性貧血	0	1 (0.5)	0
白血球減少症	0	0	2 (0.9)
リンパ球増加症	0	0	1 (0.5)
リンパ球減少症	0	0	2 (0.9)
好中球減少症	0	1 (0.5)	2 (0.9)
好中球増加症	0	1 (0.5)	0
血小板減少症	0	0	1 (0.5)
心臓障害	0	2 (0.9)	0
心房細動	0	1 (0.5)	0
心肺停止	0	1 (0.5)	0
心室細動	0	1 (0.5)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
先天性、家族性および遺伝性障害	1 (0.5)	0	0
ミトコンドリアミオパチー	1 (0.5)	0	0
耳および迷路障害	0	1 (0.5)	0
回転性めまい	0	1 (0.5)	0
眼障害	0	0	1 (0.5)
一過性黒内障	0	0	1 (0.5)
胃腸障害	7 (3.3)	5 (2.4)	14 (6.4)
腹部不快感	1 (0.5)	0	0
腹痛	0	1 (0.5)	2 (0.9)
上腹部痛	0	0	1 (0.5)
大腸炎	0	0	1 (0.5)
便秘	0	1 (0.5)	0
下痢	4 (1.9)	0	3 (1.4)
口内乾燥	1 (0.5)	1 (0.5)	0
消化不良	0	0	2 (0.9)
鼓腸	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
胃腸障害 (Cont.)			
胃出血	0	0	1 (0.5)
胃炎	0	0	1 (0.5)
びらん性胃炎	0	1 (0.5)	0
胃腸障害	1 (0.5)	0	0
痔核	0	0	1 (0.5)
口腔内潰瘍形成	0	0	2 (0.9)
悪心	3 (1.4)	1 (0.5)	2 (0.9)
小腸出血	0	0	1 (0.5)
小腸潰瘍	0	0	1 (0.5)
舌腫脹	1 (0.5)	0	0
嘔吐	1 (0.5)	0	3 (1.4)
一般・全身障害および投与部位の状態	5 (2.4)	1 (0.5)	4 (1.8)
胸痛	1 (0.5)	1 (0.5)	0
疲労	1 (0.5)	0	2 (0.9)
倦怠感	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
非心臓性胸痛	0	0	1 (0.5)
疼痛	1 (0.5)	0	0
末梢腫脹	1 (0.5)	0	0
全身性炎症反応症候群	0	0	1 (0.5)
肝胆道系障害	0	0	1 (0.5)
肝損傷	0	0	1 (0.5)
免疫系障害	1 (0.5)	0	0
季節性アレルギー	1 (0.5)	0	0
感染症および寄生虫症	28 (13.2)	33 (15.6)	41 (18.8)
膿瘍	1 (0.5)	0	0
四肢膿瘍	0	0	1 (0.5)
急性副鼻腔炎	0	0	1 (0.5)
細菌性膣症	0	1 (0.5)	0
気管支炎	1 (0.5)	5 (2.4)	3 (1.4)
蜂巣炎	0	0	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
感染症および寄生虫症 (Cont.)			
眼窩蜂巣炎	1 (0.5)	0	0
ウイルス性結膜炎	0	1 (0.5)	0
膀胱炎	1 (0.5)	1 (0.5)	0
毛嚢虫症	0	0	1 (0.5)
精巣上体炎	0	0	1 (0.5)
大腸菌性尿路感染	1 (0.5)	0	0
毛包炎	0	1 (0.5)	0
真菌感染	0	1 (0.5)	0
皮膚真菌感染	0	0	1 (0.5)
せつ	1 (0.5)	0	0
胃腸炎	1 (0.5)	0	1 (0.5)
単純ヘルペス	0	1 (0.5)	1 (0.5)
帯状疱疹	0	3 (1.4)	8 (3.7)
感染性皮膚嚢腫	1 (0.5)	0	0
インフルエンザ	0	3 (1.4)	3 (1.4)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
感染症および寄生虫症 (Cont.)			
肺感染	1 (0.5)	0	0
爪感染	0	1 (0.5)	0
上咽頭炎	2 (0.9)	2 (0.9)	1 (0.5)
口腔カンジダ症	0	0	1 (0.5)
口腔ヘルペス	0	0	1 (0.5)
中咽頭カンジダ症	0	0	1 (0.5)
中耳炎	0	0	1 (0.5)
歯周炎	1 (0.5)	0	0
咽頭炎	1 (0.5)	1 (0.5)	1 (0.5)
レンサ球菌性咽頭炎	0	2 (0.9)	2 (0.9)
肺炎	1 (0.5)	1 (0.5)	2 (0.9)
気道感染	1 (0.5)	0	1 (0.5)
ウイルス性気道感染	1 (0.5)	0	0
鼻炎	0	1 (0.5)	0
副鼻腔炎	7 (3.3)	3 (1.4)	2 (0.9)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
感染症および寄生虫症 (Cont.)			
細菌性副鼻腔炎	2 (0.9)	0	0
皮膚カンジダ	0	0	1 (0.5)
足部白癬	0	1 (0.5)	2 (0.9)
癜風	1 (0.5)	0	0
扁桃炎	0	0	1 (0.5)
歯感染	0	0	1 (0.5)
上気道感染	3 (1.4)	4 (1.9)	9 (4.1)
尿路感染	5 (2.4)	6 (2.8)	6 (2.8)
腸球菌性尿路感染	0	1 (0.5)	0
ウイルス性筋炎	0	1 (0.5)	0
ウイルス性上気道感染	0	1 (0.5)	0
外陰部腟カンジダ症	1 (0.5)	0	0
傷害、中毒および処置合併症	1 (0.5)	0	0
歯牙破折	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
臨床検査	7 (3.3)	9 (4.3)	26 (11.9)
アラニンアミノトランスフェラーゼ増加	1 (0.5)	1 (0.5)	7 (3.2)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.5)	0	6 (2.8)
血中コレステロール増加	0	1 (0.5)	0
血中クレアチンホスホキナーゼMB増加	1 (0.5)	0	0
血中クレアチンホスホキナーゼ増加	4 (1.9)	2 (0.9)	9 (4.1)
血中クレアチニン増加	0	0	1 (0.5)
血中尿素増加	0	0	1 (0.5)
血中尿酸増加	0	0	1 (0.5)
ヘマトクリット減少	0	1 (0.5)	0
ヘモグロビン減少	1 (0.5)	1 (0.5)	2 (0.9)
肝酵素上昇	0	0	4 (1.8)
肝機能検査値上昇	0	0	1 (0.5)
リンパ球数減少	0	2 (0.9)	0
リンパ球数増加	0	0	1 (0.5)
骨髄球数増加	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
臨床検査 (Cont.)			
好中球数減少	0	0	4 (1.8)
赤血球数減少	0	1 (0.5)	0
体重減少	0	0	1 (0.5)
体重増加	0	1 (0.5)	0
白血球数減少	0	2 (0.9)	1 (0.5)
代謝および栄養障害	1 (0.5)	2 (0.9)	3 (1.4)
脂質異常症	0	0	1 (0.5)
高脂血症	0	1 (0.5)	0
高トリグリセリド血症	1 (0.5)	1 (0.5)	1 (0.5)
低血糖	0	0	1 (0.5)
筋骨格系および結合組織障害	2 (0.9)	5 (2.4)	2 (0.9)
関節痛	0	1 (0.5)	0
背部痛	1 (0.5)	0	0
筋痙縮	0	1 (0.5)	0
筋肉痛	0	1 (0.5)	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
筋骨格系および結合組織障害 (Cont.)			
四肢痛	0	0	1 (0.5)
乾癬性関節症	1 (0.5)	2 (0.9)	0
急速進行性変形性関節症	0	1 (0.5)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (0.5)	1 (0.5)
直腸腺癌	0	0	1 (0.5)
直腸癌	0	1 (0.5)	0
神経系障害	4 (1.9)	3 (1.4)	7 (3.2)
浮動性めまい	1 (0.5)	1 (0.5)	1 (0.5)
頭痛	2 (0.9)	1 (0.5)	5 (2.3)
感覚鈍麻	0	1 (0.5)	0
片頭痛	1 (0.5)	0	0
ヘルペス後神経痛	0	0	1 (0.5)
失神寸前の状態	0	0	1 (0.5)
精神障害	2 (0.9)	0	2 (0.9)
感情不安定	0	0	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
精神障害 (Cont.)			
不安	1 (0.5)	0	0
うつ病	0	0	1 (0.5)
悪夢	1 (0.5)	0	0
生殖系および乳房障害	1 (0.5)	0	0
腟分泌物	1 (0.5)	0	0
呼吸器、胸郭および縦隔障害	3 (1.4)	4 (1.9)	3 (1.4)
急性呼吸不全	0	1 (0.5)	1 (0.5)
咳嗽	1 (0.5)	1 (0.5)	1 (0.5)
呼吸困難	0	0	1 (0.5)
労作性呼吸困難	0	1 (0.5)	0
鼻出血	1 (0.5)	0	0
口腔咽頭痛	0	0	1 (0.5)
肺塞栓症	0	1 (0.5)	0
副鼻腔うっ血	0	1 (0.5)	0
声帯障害	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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Program Source Code: [redacted]

TABLE 14.3__1.6.1

Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term - up to Week 24
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
皮膚および皮下組織障害	5 (2.4)	3 (1.4)	5 (2.3)
ざ瘡	1 (0.5)	3 (1.4)	2 (0.9)
脱毛症	0	0	1 (0.5)
斑状出血	0	0	1 (0.5)
光線過敏性反応	1 (0.5)	0	0
乾癬	2 (0.9)	0	0
発疹	1 (0.5)	0	1 (0.5)
血管障害	2 (0.9)	1 (0.5)	0
高血圧	2 (0.9)	1 (0.5)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

表 3.　　長期投与時の有害事象の 100 人年あたりの発現件数：MedDRA のプライマリー器官別大分類及び基本語別（安全性解析対象集団）

相互参照：M15-554 試験 CSR W24 Table 14.3__1.2.2

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
Any adverse event	840 (286.9)	1105 (373.1)
血液およびリンパ系障害	13 (4.4)	36 (12.2)
貧血	3 (1.0)	13 (4.4)
失血性貧血	1 (0.3)	1 (0.3)
血球減少症	0	1 (0.3)
播種性血管内凝固	0	1 (0.3)
内出血発生の増加傾向	1 (0.3)	0
鉄欠乏性貧血	2 (0.7)	1 (0.3)
白血球減少症	0	3 (1.0)
リンパ節炎	0	1 (0.3)
リンパ球増加症	0	1 (0.3)
リンパ球減少症	1 (0.3)	4 (1.4)
好中球減少症	4 (1.4)	6 (2.0)
好中球増加症	1 (0.3)	0
汎血球減少症	0	1 (0.3)
脾肉芽腫	0	1 (0.3)
血小板減少症	0	1 (0.3)
血小板増加症	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
心臓障害	17 (5.8)	12 (4.1)
急性心筋梗塞	1 (0.3)	0
狭心症	1 (0.3)	0
不安定狭心症	0	1 (0.3)
心房細動	1 (0.3)	2 (0.7)
第一度房室ブロック	1 (0.3)	0
徐脈	3 (1.0)	1 (0.3)
心肺停止	1 (0.3)	0
心拡大	0	1 (0.3)
心腎症候群	0	1 (0.3)
冠動脈狭窄	0	1 (0.3)
左室肥大	0	1 (0.3)
心筋梗塞	1 (0.3)	0
動悸	6 (2.0)	0
起立性頻脈症候群	0	1 (0.3)
洞性徐脈	0	1 (0.3)
洞性頻脈	0	1 (0.3)
上室性頻脈	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
心臓障害 (Cont.)		
頻脈	1 (0.3)	0
心室細動	1 (0.3)	0
先天性、家族性および遺伝性障害	0	2 (0.7)
胃腸管動静脈奇形	0	1 (0.3)
陰嚢水瘤	0	1 (0.3)
耳および迷路障害	5 (1.7)	4 (1.4)
耳不快感	0	1 (0.3)
耳痛	1 (0.3)	0
回転性めまい	3 (1.0)	3 (1.0)
頭位性回転性めまい	1 (0.3)	0
内分泌障害	3 (1.0)	9 (3.0)
自己免疫性甲状腺炎	0	2 (0.7)
甲状腺腫	1 (0.3)	1 (0.3)
甲状腺機能亢進症	0	1 (0.3)
甲状腺機能低下症	2 (0.7)	3 (1.0)
甲状腺腫瘤	0	2 (0.7)
眼障害	7 (2.4)	13 (4.4)
一過性黒内障	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
眼障害 (Cont.)		
閉塞隅角緑内障	1 (0.3)	0
眼精疲労	0	1 (0.3)
眼瞼炎	0	1 (0.3)
白内障	1 (0.3)	3 (1.0)
霰粒腫	1 (0.3)	2 (0.7)
アレルギー性結膜炎	1 (0.3)	0
眼痛	0	1 (0.3)
緑内障	0	1 (0.3)
水晶体脱臼	0	1 (0.3)
眼部不快感	0	1 (0.3)
後嚢部混濁	1 (0.3)	0
眼瞼腫脹	0	1 (0.3)
霧視	1 (0.3)	0
視力障害	1 (0.3)	0
胃腸障害	82 (28.0)	118 (39.8)
腹部不快感	6 (2.0)	2 (0.7)
腹部膨満	3 (1.0)	1 (0.3)
腹痛	7 (2.4)	5 (1.7)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
胃腸障害 (Cont.)		
上腹部痛	3 (1.0)	4 (1.4)
アフタ性潰瘍	0	2 (0.7)
腹水	0	1 (0.3)
バレット食道	1 (0.3)	0
大腸炎	0	2 (0.7)
便秘	8 (2.7)	9 (3.0)
クローン病	1 (0.3)	0
齲歯	1 (0.3)	1 (0.3)
下痢	11 (3.8)	22 (7.4)
憩室	0	1 (0.3)
腸憩室	0	1 (0.3)
口内乾燥	2 (0.7)	2 (0.7)
十二指腸潰瘍	1 (0.3)	1 (0.3)
出血性十二指腸潰瘍	0	1 (0.3)
消化不良	5 (1.7)	5 (1.7)
嚥下障害	0	3 (1.0)
食中毒	1 (0.3)	1 (0.3)
胃出血	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
胃腸障害 (Cont.)		
胃炎	1 (0.3)	3 (1.0)
びらん性胃炎	1 (0.3)	0
消化器痛	0	1 (0.3)
胃食道逆流性疾患	2 (0.7)	2 (0.7)
歯肉退縮	1 (0.3)	0
潰瘍性歯肉炎	0	1 (0.3)
吐血	0	1 (0.3)
痔出血	1 (0.3)	0
痔核	4 (1.4)	3 (1.0)
鼠径ヘルニア	0	1 (0.3)
大腸ポリープ	0	1 (0.3)
腰ヘルニア	1 (0.3)	0
口腔内潰瘍形成	2 (0.7)	2 (0.7)
悪心	9 (3.1)	14 (4.7)
口腔粘膜水疱形成	1 (0.3)	0
膵脂肪変性	0	1 (0.3)
急性膵炎	0	1 (0.3)
直腸出血	1 (0.3)	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
胃腸障害 (Cont.)		
直腸潰瘍	1 (0.3)	0
小腸出血	0	1 (0.3)
小腸潰瘍	0	1 (0.3)
口内炎	1 (0.3)	7 (2.4)
歯痛	1 (0.3)	3 (1.0)
臍ヘルニア	2 (0.7)	0
嘔吐	3 (1.0)	9 (3.0)
一般・全身障害および投与部位の状態	25 (8.5)	31 (10.5)
医薬品副作用	1 (0.3)	0
無力症	0	1 (0.3)
腋窩痛	1 (0.3)	0
胸部不快感	0	1 (0.3)
胸痛	1 (0.3)	1 (0.3)
悪寒	1 (0.3)	1 (0.3)
薬物不耐性	2 (0.7)	3 (1.0)
疲労	5 (1.7)	7 (2.4)
インフルエンザ様疾患	0	1 (0.3)
倦怠感	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)		
医療機器使用部位関節腫脹	0	1 (0.3)
非心臓性胸痛	0	1 (0.3)
末梢性浮腫	6 (2.0)	5 (1.7)
疼痛	0	1 (0.3)
末梢腫脹	0	1 (0.3)
発熱	7 (2.4)	6 (2.0)
全身性炎症反応症候群	0	1 (0.3)
肝胆道系障害	6 (2.0)	17 (5.7)
慢性胆嚢炎	0	1 (0.3)
胆石症	1 (0.3)	4 (1.4)
胆嚢ポリープ	0	1 (0.3)
肝硬変	0	1 (0.3)
肝嚢胞	0	3 (1.0)
肝機能異常	1 (0.3)	0
脂肪肝	1 (0.3)	5 (1.7)
高ビリルビン血症	2 (0.7)	0
過形成性胆嚢症	0	1 (0.3)
肝損傷	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
肝胆道系障害 (Cont.)		
胆管穿孔	1 (0.3)	0
免疫系障害	4 (1.4)	6 (2.0)
造影剤アレルギー	0	1 (0.3)
薬物過敏症	0	3 (1.0)
過敏症	1 (0.3)	0
季節性アレルギー	3 (1.0)	2 (0.7)
感染症および寄生虫症	282 (96.3)	352 (118.8)
膿瘍	2 (0.7)	0
四肢膿瘍	0	2 (0.7)
急性副鼻腔炎	2 (0.7)	2 (0.7)
肛門膿瘍	1 (0.3)	0
肛門カンジダ症	1 (0.3)	0
肛門直腸蜂巣炎	0	1 (0.3)
菌血症	0	1 (0.3)
細菌性膣症	2 (0.7)	0
細菌尿	0	2 (0.7)
体部白癬	1 (0.3)	0
細気管支炎	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)		
気管支炎	26 (8.9)	24 (8.1)
カンジダ感染	0	1 (0.3)
気管カンジダ症	0	1 (0.3)
蜂巣炎	5 (1.7)	9 (3.0)
コクシジオイデス症	1 (0.3)	0
ウイルス性結膜炎	1 (0.3)	0
クリプトスポリジウム感染	1 (0.3)	0
膀胱炎	2 (0.7)	5 (1.7)
サイトメガロウイルス感染	0	1 (0.3)
毛嚢虫症	0	1 (0.3)
爪の皮膚糸状菌症	0	1 (0.3)
憩室炎	0	3 (1.0)
耳感染	3 (1.0)	2 (0.7)
エンテロウイルス感染	0	1 (0.3)
精巣上体炎	0	1 (0.3)
大腸菌感染	1 (0.3)	0
硬膜外膿瘍	0	1 (0.3)
眼感染	1 (0.3)	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)		
毛包炎	5 (1.7)	7 (2.4)
真菌感染	1 (0.3)	0
皮膚真菌感染	0	3 (1.0)
せつ	0	1 (0.3)
胃腸炎	5 (1.7)	11 (3.7)
ウイルス性胃腸炎	8 (2.7)	7 (2.4)
陰部ヘルペス	1 (0.3)	1 (0.3)
ジアルジア症	1 (0.3)	0
歯肉膿瘍	0	1 (0.3)
歯肉炎	0	1 (0.3)
単純ヘルペス	2 (0.7)	2 (0.7)
帯状疱疹	10 (3.4)	25 (8.4)
麦粒腫	0	2 (0.7)
膿痂疹	0	1 (0.3)
インフルエンザ	19 (6.5)	19 (6.4)
腎感染	0	1 (0.3)
喉頭炎	1 (0.3)	1 (0.3)
潜伏結核	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)		
下気道感染	1 (0.3)	1 (0.3)
肺感染	1 (0.3)	1 (0.3)
爪感染	2 (0.7)	0
上咽頭炎	32 (10.9)	44 (14.9)
食道カンジダ症	1 (0.3)	0
爪真菌症	1 (0.3)	0
口腔カンジダ症	2 (0.7)	5 (1.7)
口腔ヘルペス	2 (0.7)	7 (2.4)
中咽頭カンジダ症	0	1 (0.3)
外耳炎	1 (0.3)	2 (0.7)
中耳炎	2 (0.7)	3 (1.0)
急性中耳炎	1 (0.3)	0
歯冠周囲炎	1 (0.3)	0
歯周炎	0	1 (0.3)
咽頭炎	5 (1.7)	10 (3.4)
レンサ球菌性咽頭炎	4 (1.4)	2 (0.7)
ニューモシスチス・イロベチイ肺炎	0	1 (0.3)
肺炎	7 (2.4)	7 (2.4)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)		
細菌性肺炎	0	1 (0.3)
処置後蜂巣炎	1 (0.3)	0
シュードモナス感染	0	1 (0.3)
歯髄炎	1 (0.3)	0
膿尿	1 (0.3)	1 (0.3)
気道感染	2 (0.7)	5 (1.7)
ウイルス性気道感染	1 (0.3)	0
鼻炎	1 (0.3)	1 (0.3)
敗血症	0	1 (0.3)
副鼻腔炎	17 (5.8)	12 (4.1)
皮膚カンジダ	1 (0.3)	2 (0.7)
皮膚感染	0	1 (0.3)
ブドウ球菌皮膚感染	1 (0.3)	0
皮下組織膿瘍	2 (0.7)	0
股部白癬	0	1 (0.3)
白癬感染	0	2 (0.7)
足部白癬	2 (0.7)	2 (0.7)
扁桃炎	1 (0.3)	3 (1.0)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)		
歯膿瘍	2 (0.7)	2 (0.7)
歯感染	4 (1.4)	5 (1.7)
気管気管支炎	0	1 (0.3)
細菌性気管気管支炎	0	1 (0.3)
上気道感染	38 (13.0)	41 (13.8)
尿路感染	31 (10.6)	25 (8.4)
細菌性尿路感染	1 (0.3)	0
腸球菌性尿路感染	1 (0.3)	0
ウイルス感染	0	4 (1.4)
ウイルス性筋炎	1 (0.3)	0
ウイルス性発疹	0	1 (0.3)
ウイルス性扁桃炎	1 (0.3)	0
ウイルス性上気道感染	5 (1.7)	6 (2.0)
外陰部腟カンジダ症	0	4 (1.4)
傷害、中毒および処置合併症	65 (22.2)	59 (19.9)
動物咬傷	1 (0.3)	3 (1.0)
足関節部骨折	1 (0.3)	1 (0.3)
節足動物咬傷	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)		
剥離骨折	1 (0.3)	0
骨亀裂	1 (0.3)	0
第2度熱傷	0	1 (0.3)
軟骨損傷	1 (0.3)	0
頚椎骨折	1 (0.3)	0
化学熱傷	0	1 (0.3)
挫傷	8 (2.7)	7 (2.4)
角膜擦過傷	1 (0.3)	1 (0.3)
上顆炎	1 (0.3)	0
眼挫傷	0	1 (0.3)
転倒	5 (1.7)	7 (2.4)
大腿骨頚部骨折	0	1 (0.3)
足骨折	3 (1.0)	1 (0.3)
凍傷	0	1 (0.3)
手骨折	1 (0.3)	0
損傷	1 (0.3)	0
関節脱臼	1 (0.3)	0
関節損傷	2 (0.7)	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)		
靭帯断裂	1 (0.3)	0
靭帯捻挫	2 (0.7)	2 (0.7)
四肢圧挫損傷	1 (0.3)	0
四肢損傷	3 (1.0)	2 (0.7)
腰椎骨折	1 (0.3)	0
つち指	1 (0.3)	0
半月板損傷	2 (0.7)	1 (0.3)
筋損傷	0	1 (0.3)
肉離れ	3 (1.0)	2 (0.7)
膝蓋骨骨折	1 (0.3)	0
処置後胆汁漏出	1 (0.3)	0
処置による疼痛	3 (1.0)	2 (0.7)
肋骨骨折	0	2 (0.7)
交通事故	3 (1.0)	0
皮膚擦過傷	0	1 (0.3)
皮膚裂傷	4 (1.4)	5 (1.7)
脊椎圧迫骨折	0	3 (1.0)
胸骨骨折	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)		
ストレス骨折	0	1 (0.3)
腱損傷	1 (0.3)	1 (0.3)
腱断裂	2 (0.7)	1 (0.3)
熱傷	0	2 (0.7)
胸椎骨折	1 (0.3)	0
歯牙破折	2 (0.7)	4 (1.4)
外傷性関節炎	1 (0.3)	0
外傷性血胸	1 (0.3)	0
上肢骨折	1 (0.3)	1 (0.3)
手首関節骨折	1 (0.3)	0
臨床検査	63 (21.5)	111 (37.5)
アラニンアミノトランスフェラーゼ増加	4 (1.4)	20 (6.8)
抗甲状腺抗体陽性	1 (0.3)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.3)	13 (4.4)
血中アルカリホスファターゼ増加	1 (0.3)	1 (0.3)
血中ビリルビン増加	1 (0.3)	1 (0.3)
血中コレステロール増加	2 (0.7)	1 (0.3)
血中クレアチン増加	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
臨床検査 (Cont.)		
血中クレアチンホスホキナーゼ増加	18 (6.1)	27 (9.1)
血中クレアチニン増加	1 (0.3)	2 (0.7)
血中葉酸減少	1 (0.3)	0
血中ブドウ糖増加	2 (0.7)	2 (0.7)
血中カリウム増加	1 (0.3)	2 (0.7)
血圧上昇	1 (0.3)	2 (0.7)
収縮期血圧上昇	0	1 (0.3)
血中テストステロン減少	1 (0.3)	2 (0.7)
血中トリグリセリド増加	0	1 (0.3)
血中尿素増加	1 (0.3)	1 (0.3)
血中尿酸増加	1 (0.3)	1 (0.3)
体温上昇	1 (0.3)	0
心雑音	0	1 (0.3)
ヘマトクリット減少	1 (0.3)	1 (0.3)
ヘモグロビン減少	1 (0.3)	3 (1.0)
心拍数減少	1 (0.3)	0
肝酵素上昇	2 (0.7)	5 (1.7)
深吸気量減少	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
臨床検査 (Cont.)		
肝機能検査値上昇	1 (0.3)	3 (1.0)
低比重リポ蛋白増加	0	1 (0.3)
リンパ球数減少	2 (0.7)	0
リンパ球数増加	0	1 (0.3)
リンパ球形態異常	2 (0.7)	0
好中球数減少	0	6 (2.0)
好中球数増加	2 (0.7)	0
赤血球数減少	1 (0.3)	1 (0.3)
トランスアミナーゼ上昇	2 (0.7)	2 (0.7)
超低比重リポ蛋白増加	0	1 (0.3)
体重減少	0	1 (0.3)
体重増加	4 (1.4)	4 (1.4)
白血球数減少	3 (1.0)	3 (1.0)
白血球数増加	2 (0.7)	0
代謝および栄養障害	30 (10.2)	30 (10.1)
異常体重減少	0	1 (0.3)
食欲減退	0	1 (0.3)
脱水	0	2 (0.7)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)		
糖尿病	5 (1.7)	0
脂質異常症	0	2 (0.7)
耐糖能障害	1 (0.3)	0
高カルシウム血症	0	1 (0.3)
高コレステロール血症	3 (1.0)	2 (0.7)
高血糖	1 (0.3)	2 (0.7)
高カリウム血症	2 (0.7)	0
高脂血症	9 (3.1)	2 (0.7)
高トリグリセリド血症	2 (0.7)	3 (1.0)
低血糖	0	2 (0.7)
低カリウム血症	1 (0.3)	0
低ナトリウム血症	1 (0.3)	0
栄養障害	0	1 (0.3)
2型糖尿病	0	4 (1.4)
ビタミンB12欠乏	2 (0.7)	2 (0.7)
ビタミンD欠乏	3 (1.0)	5 (1.7)
筋骨格系および結合組織障害	85 (29.0)	66 (22.3)
関節痛	12 (4.1)	9 (3.0)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)		
背部痛	14 (4.8)	9 (3.0)
滑液包炎	3 (1.0)	4 (1.4)
尾骨痛	0	1 (0.3)
外骨腫	0	1 (0.3)
顎骨の外骨腫	0	1 (0.3)
顔面非対称	1 (0.3)	0
側腹部痛	1 (0.3)	0
椎間板変性症	1 (0.3)	0
椎間板障害	1 (0.3)	0
椎間板突出	1 (0.3)	2 (0.7)
関節滲出液	0	1 (0.3)
関節腫脹	1 (0.3)	1 (0.3)
筋痙縮	6 (2.0)	4 (1.4)
筋肉痛	2 (0.7)	3 (1.0)
頚部痛	0	3 (1.0)
変形性関節症	7 (2.4)	4 (1.4)
骨壊死	1 (0.3)	0
骨減少症	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)		
骨粗鬆症	1 (0.3)	1 (0.3)
四肢痛	0	2 (0.7)
足底筋膜炎	0	1 (0.3)
多発性関節炎	0	1 (0.3)
乾癬性関節症	17 (5.8)	9 (3.0)
急速進行性変形性関節症	1 (0.3)	0
関節リウマチ	0	1 (0.3)
肩回旋筋腱板症候群	2 (0.7)	2 (0.7)
側弯症	0	1 (0.3)
変形性脊椎症	0	1 (0.3)
脊椎痛	0	1 (0.3)
脊柱管狭窄症	0	1 (0.3)
滑液嚢腫	4 (1.4)	0
全身性エリテマトーデス	1 (0.3)	0
顎関節症候群	2 (0.7)	0
腱炎	3 (1.0)	0
腱鞘炎	1 (0.3)	1 (0.3)
狭窄性腱鞘炎	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)		
胸部脊柱管狭窄症	0	1 (0.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	9 (3.1)	13 (4.4)
肛門性器疣贅	0	2 (0.7)
基底細胞癌	3 (1.0)	1 (0.3)
基底扁平上皮癌	0	1 (0.3)
大腸腺腫	1 (0.3)	1 (0.3)
子宮内膜癌	0	1 (0.3)
乳管内乳頭腫	0	1 (0.3)
脂肪腫	0	1 (0.3)
悪性黒色腫	0	1 (0.3)
悪性黒色腫第3期	1 (0.3)	0
中咽頭扁平上皮癌	0	1 (0.3)
卵巣癌	0	1 (0.3)
前立腺癌	2 (0.7)	0
直腸腺癌	0	1 (0.3)
直腸癌	1 (0.3)	0
扁平上皮癌	0	1 (0.3)
子宮平滑筋腫	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
神経系障害	30 (10.2)	59 (19.9)
手根管症候群	2 (0.7)	5 (1.7)
脳梗塞	0	1 (0.3)
頚髄神経根障害	1 (0.3)	2 (0.7)
頚腕症候群	3 (1.0)	0
糖尿病性ニューロパチー	0	2 (0.7)
浮動性めまい	5 (1.7)	8 (2.7)
顔面麻痺	0	1 (0.3)
頭部不快感	0	1 (0.3)
頭痛	6 (2.0)	11 (3.7)
知覚過敏	1 (0.3)	0
感覚鈍麻	2 (0.7)	3 (1.0)
肋間神経痛	0	1 (0.3)
腰仙部神経根障害	0	1 (0.3)
片頭痛	2 (0.7)	4 (1.4)
モートン神経痛	1 (0.3)	0
神経圧迫	0	1 (0.3)
末梢性ニューロパチー	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
神経系障害 (Cont.)		
錯感覚	1 (0.3)	1 (0.3)
腓骨神経麻痺	1 (0.3)	0
ヘルペス後神経痛	1 (0.3)	6 (2.0)
失神寸前の状態	0	1 (0.3)
坐骨神経痛	0	2 (0.7)
会話障害	1 (0.3)	0
失神	1 (0.3)	4 (1.4)
緊張性頭痛	0	1 (0.3)
胸髄神経根障害	0	1 (0.3)
一過性全健忘	0	1 (0.3)
振戦	2 (0.7)	0
妊娠、産褥および周産期の状態	0	1 (0.3)
異所性妊娠	0	1 (0.3)
精神障害	20 (6.8)	26 (8.8)
抑うつ気分を伴う適応障害	1 (0.3)	0
感情不安定	0	1 (0.3)
不安	6 (2.0)	4 (1.4)
不安障害	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
精神障害 (Cont.)		
双極性障害	1 (0.3)	0
うつ病	7 (2.4)	11 (3.7)
失見当識	1 (0.3)	0
薬物乱用	0	1 (0.3)
不眠症	3 (1.0)	3 (1.0)
リビドー減退	0	1 (0.3)
大うつ病	0	1 (0.3)
精神状態変化	0	1 (0.3)
パニック発作	1 (0.3)	1 (0.3)
ストレス	0	1 (0.3)
腎および尿路障害	14 (4.8)	15 (5.1)
急性腎障害	1 (0.3)	1 (0.3)
膀胱拡大	0	1 (0.3)
膀胱結石	0	1 (0.3)
着色尿	0	1 (0.3)
慢性腎臓病	0	1 (0.3)
排尿困難	0	1 (0.3)
血尿	3 (1.0)	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)		
白血球尿	1 (0.3)	2 (0.7)
腎結石症	3 (1.0)	3 (1.0)
蛋白尿	1 (0.3)	1 (0.3)
腎仙痛	3 (1.0)	0
腎嚢胞	0	2 (0.7)
腹圧性尿失禁	1 (0.3)	0
尿失禁	1 (0.3)	0
生殖系および乳房障害	10 (3.4)	9 (3.0)
子宮付属器嚢胞	0	1 (0.3)
亀頭包皮炎	1 (0.3)	0
良性前立腺肥大症	1 (0.3)	2 (0.7)
乳房腫瘤	0	2 (0.7)
子宮頚部上皮異形成	1 (0.3)	0
機能不全性子宮出血	1 (0.3)	0
勃起不全	0	1 (0.3)
月経過多	1 (0.3)	0
不規則月経	1 (0.3)	0
卵巣嚢胞	1 (0.3)	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)		
前立腺石灰化	0	1 (0.3)
前立腺炎	1 (0.3)	1 (0.3)
腟異形成	1 (0.3)	0
腟出血	1 (0.3)	0
呼吸器、胸郭および縦隔障害	23 (7.9)	38 (12.8)
急性呼吸不全	1 (0.3)	1 (0.3)
喘息	0	4 (1.4)
気管支反応性亢進	2 (0.7)	0
慢性閉塞性肺疾患	0	5 (1.7)
咳嗽	6 (2.0)	9 (3.0)
呼吸困難	1 (0.3)	1 (0.3)
労作性呼吸困難	1 (0.3)	0
鼻出血	1 (0.3)	0
間質性肺疾患	0	1 (0.3)
鼻閉	0	1 (0.3)
口腔咽頭痛	4 (1.4)	7 (2.4)
呼吸時疼痛	1 (0.3)	0
副鼻腔嚢胞	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)		
胸水	0	1 (0.3)
気胸	0	1 (0.3)
湿性咳嗽	0	1 (0.3)
肺塞栓症	1 (0.3)	0
肺腫瘤	0	1 (0.3)
逆流性喉頭炎	0	1 (0.3)
気道うっ血	2 (0.7)	1 (0.3)
アレルギー性鼻炎	1 (0.3)	0
副鼻腔うっ血	1 (0.3)	1 (0.3)
咽喉刺激感	0	1 (0.3)
上気道の炎症	0	1 (0.3)
皮膚および皮下組織障害	29 (9.9)	56 (18.9)
ざ瘡	4 (1.4)	7 (2.4)
光線角化症	0	1 (0.3)
脱毛症	0	4 (1.4)
皮脂欠乏症	0	1 (0.3)
水疱	0	1 (0.3)
皮膚炎	2 (0.7)	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)		
アトピー性皮膚炎	0	1 (0.3)
接触皮膚炎	1 (0.3)	0
薬疹	0	3 (1.0)
異汗性湿疹	0	1 (0.3)
斑状出血	1 (0.3)	3 (1.0)
湿疹	1 (0.3)	1 (0.3)
多汗症	1 (0.3)	0
内方発育毛	1 (0.3)	0
汗疹	1 (0.3)	2 (0.7)
爪乾癬	1 (0.3)	0
寝汗	0	2 (0.7)
爪痛	1 (0.3)	0
乾癬	6 (2.0)	5 (1.7)
老人性紫斑	1 (0.3)	0
発疹	1 (0.3)	9 (3.0)
紅斑性皮疹	0	1 (0.3)
斑状皮疹	1 (0.3)	0
そう痒性皮疹	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2.2

Treatment-Emergent Adverse Events per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)		
小水疱性皮疹	1 (0.3)	0
酒さ	1 (0.3)	5 (1.7)
脂漏性皮膚炎	1 (0.3)	1 (0.3)
皮膚変色	0	1 (0.3)
皮膚病変	1 (0.3)	3 (1.0)
皮膚潰瘍	1 (0.3)	0
蕁麻疹	1 (0.3)	2 (0.7)
血管障害	18 (6.1)	22 (7.4)
本態性高血圧症	1 (0.3)	0
大腿動脈瘤	0	1 (0.3)
高血圧	16 (5.5)	16 (5.4)
低血圧	1 (0.3)	3 (1.0)
表在性血栓性静脈炎	0	1 (0.3)
四肢静脈血栓症	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

表 4. 長期投与時の治験薬と関連ありの有害事象の 100 人年あたりの発現件数：MedDRA のプライマリー器官別大分類及び基本語別（安全性解析対象集団）

相互参照：M15-554 試験 CSR W24 Table 14.3__1.6.2

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
Any adverse event	207 (70.7)	346 (116.8)
血液およびリンパ系障害	8 (2.7)	23 (7.8)
貧血	3 (1.0)	6 (2.0)
失血性貧血	1 (0.3)	1 (0.3)
血球減少症	0	1 (0.3)
播種性血管内凝固	0	1 (0.3)
白血球減少症	0	3 (1.0)
リンパ節炎	0	1 (0.3)
リンパ球増加症	0	1 (0.3)
リンパ球減少症	0	3 (1.0)
好中球減少症	3 (1.0)	4 (1.4)
好中球増加症	1 (0.3)	0
汎血球減少症	0	1 (0.3)
血小板減少症	0	1 (0.3)
心臓障害	3 (1.0)	0
心房細動	1 (0.3)	0
心肺停止	1 (0.3)	0
心室細動	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
耳および迷路障害	2 (0.7)	0
耳痛	1 (0.3)	0
回転性めまい	1 (0.3)	0
眼障害	0	2 (0.7)
一過性黒内障	0	1 (0.3)
霰粒腫	0	1 (0.3)
胃腸障害	13 (4.4)	33 (11.1)
腹部不快感	0	1 (0.3)
腹痛	4 (1.4)	2 (0.7)
上腹部痛	0	2 (0.7)
大腸炎	0	2 (0.7)
便秘	1 (0.3)	0
下痢	2 (0.7)	4 (1.4)
口内乾燥	1 (0.3)	0
十二指腸潰瘍	0	1 (0.3)
消化不良	0	2 (0.7)
胃出血	0	1 (0.3)
胃炎	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
胃腸障害 (Cont.)		
びらん性胃炎	1 (0.3)	0
消化器痛	0	1 (0.3)
潰瘍性歯肉炎	0	1 (0.3)
痔核	0	1 (0.3)
口腔内潰瘍形成	0	2 (0.7)
悪心	2 (0.7)	2 (0.7)
口腔粘膜水疱形成	1 (0.3)	0
膵脂肪変性	0	1 (0.3)
小腸出血	0	1 (0.3)
小腸潰瘍	0	1 (0.3)
口内炎	0	3 (1.0)
歯痛	1 (0.3)	1 (0.3)
嘔吐	0	3 (1.0)
一般・全身障害および投与部位の状態	3 (1.0)	9 (3.0)
胸痛	1 (0.3)	1 (0.3)
疲労	1 (0.3)	5 (1.7)
非心臓性胸痛	0	1 (0.3)
末梢性浮腫	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)		
発熱	0	1 (0.3)
全身性炎症反応症候群	0	1 (0.3)
肝胆道系障害	1 (0.3)	2 (0.7)
肝機能異常	1 (0.3)	0
脂肪肝	0	1 (0.3)
肝損傷	0	1 (0.3)
感染症および寄生虫症	108 (36.9)	146 (49.3)
膿瘍	1 (0.3)	0
四肢膿瘍	0	1 (0.3)
急性副鼻腔炎	1 (0.3)	2 (0.7)
肛門直腸蜂巣炎	0	1 (0.3)
細菌性膣症	1 (0.3)	0
体部白癬	1 (0.3)	0
細気管支炎	1 (0.3)	0
気管支炎	12 (4.1)	9 (3.0)
蜂巣炎	1 (0.3)	3 (1.0)
コクシジオイデス症	1 (0.3)	0
ウイルス性結膜炎	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)		
膀胱炎	1 (0.3)	0
サイトメガロウイルス感染	0	1 (0.3)
毛嚢虫症	0	1 (0.3)
憩室炎	0	2 (0.7)
耳感染	0	1 (0.3)
精巣上体炎	0	1 (0.3)
眼感染	1 (0.3)	0
毛包炎	3 (1.0)	1 (0.3)
真菌感染	1 (0.3)	0
皮膚真菌感染	0	1 (0.3)
せつ	0	1 (0.3)
胃腸炎	1 (0.3)	3 (1.0)
ウイルス性胃腸炎	1 (0.3)	2 (0.7)
歯肉膿瘍	0	1 (0.3)
単純ヘルペス	1 (0.3)	2 (0.7)
帯状疱疹	7 (2.4)	21 (7.1)
麦粒腫	0	1 (0.3)
膿痂疹	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)		
インフルエンザ	4 (1.4)	5 (1.7)
潜伏結核	0	1 (0.3)
下気道感染	1 (0.3)	0
肺感染	1 (0.3)	0
爪感染	1 (0.3)	0
上咽頭炎	7 (2.4)	7 (2.4)
口腔カンジダ症	0	1 (0.3)
口腔ヘルペス	2 (0.7)	4 (1.4)
中咽頭カンジダ症	0	1 (0.3)
外耳炎	0	1 (0.3)
中耳炎	0	2 (0.7)
咽頭炎	1 (0.3)	4 (1.4)
レンサ球菌性咽頭炎	2 (0.7)	2 (0.7)
ニューモシスチス・イロベチイ肺炎	0	1 (0.3)
肺炎	4 (1.4)	5 (1.7)
細菌性肺炎	0	1 (0.3)
シュードモナス感染	0	1 (0.3)
膿尿	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)		
気道感染	1 (0.3)	2 (0.7)
ウイルス性気道感染	1 (0.3)	0
鼻炎	1 (0.3)	0
副鼻腔炎	9 (3.1)	5 (1.7)
皮膚カンジダ	0	2 (0.7)
皮下組織膿瘍	2 (0.7)	0
股部白癬	0	1 (0.3)
白癬感染	0	1 (0.3)
足部白癬	1 (0.3)	2 (0.7)
扁桃炎	0	1 (0.3)
歯膿瘍	0	1 (0.3)
歯感染	0	2 (0.7)
細菌性気管気管支炎	0	1 (0.3)
上気道感染	12 (4.1)	19 (6.4)
尿路感染	17 (5.8)	15 (5.1)
細菌性尿路感染	1 (0.3)	0
腸球菌性尿路感染	1 (0.3)	0
ウイルス感染	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)		
ウイルス性筋炎	1 (0.3)	0
ウイルス性上気道感染	1 (0.3)	1 (0.3)
傷害、中毒および処置合併症	0	2 (0.7)
処置による疼痛	0	1 (0.3)
歯牙破折	0	1 (0.3)
臨床検査	29 (9.9)	73 (24.6)
アラニンアミノトランスフェラーゼ増加	3 (1.0)	15 (5.1)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.3)	10 (3.4)
血中アルカリホスファターゼ増加	1 (0.3)	0
血中コレステロール増加	2 (0.7)	1 (0.3)
血中クレアチン増加	1 (0.3)	0
血中クレアチンホスホキナーゼ増加	9 (3.1)	21 (7.1)
血中クレアチニン増加	1 (0.3)	1 (0.3)
血圧上昇	0	1 (0.3)
血中尿素増加	1 (0.3)	1 (0.3)
血中尿酸増加	0	1 (0.3)
体温上昇	1 (0.3)	0
ヘマトクリット減少	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
臨床検査 (Cont.)		
ヘモグロビン減少	1 (0.3)	2 (0.7)
肝酵素上昇	0	5 (1.7)
深吸気量減少	0	1 (0.3)
肝機能検査値上昇	0	3 (1.0)
低比重リポ蛋白増加	0	1 (0.3)
リンパ球数減少	2 (0.7)	0
リンパ球数増加	0	1 (0.3)
好中球数減少	0	5 (1.7)
赤血球数減少	1 (0.3)	0
トランスアミナーゼ上昇	1 (0.3)	0
体重減少	0	1 (0.3)
体重増加	1 (0.3)	1 (0.3)
白血球数減少	2 (0.7)	2 (0.7)
代謝および栄養障害	4 (1.4)	6 (2.0)
脂質異常症	0	1 (0.3)
高コレステロール血症	0	1 (0.3)
高脂血症	2 (0.7)	1 (0.3)
高トリグリセリド血症	2 (0.7)	2 (0.7)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)		
低血糖	0	1 (0.3)
筋骨格系および結合組織障害	8 (2.7)	6 (2.0)
関節痛	2 (0.7)	0
背部痛	0	1 (0.3)
筋痙縮	1 (0.3)	0
筋肉痛	1 (0.3)	1 (0.3)
変形性関節症	0	1 (0.3)
四肢痛	0	1 (0.3)
乾癬性関節症	3 (1.0)	2 (0.7)
急速進行性変形性関節症	1 (0.3)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.7)	3 (1.0)
肛門性器疣贅	0	2 (0.7)
大腸腺腫	1 (0.3)	0
直腸腺癌	0	1 (0.3)
直腸癌	1 (0.3)	0
神経系障害	4 (1.4)	15 (5.1)
頚髄神経根障害	0	1 (0.3)
浮動性めまい	1 (0.3)	2 (0.7)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
神経系障害 (Cont.)		
顔面麻痺	0	1 (0.3)
頭痛	1 (0.3)	6 (2.0)
感覚鈍麻	1 (0.3)	0
ヘルペス後神経痛	1 (0.3)	3 (1.0)
失神寸前の状態	0	1 (0.3)
失神	0	1 (0.3)
精神障害	0	2 (0.7)
感情不安定	0	1 (0.3)
うつ病	0	1 (0.3)
生殖系および乳房障害	0	1 (0.3)
前立腺炎	0	1 (0.3)
呼吸器、胸郭および縦隔障害	8 (2.7)	9 (3.0)
急性呼吸不全	1 (0.3)	1 (0.3)
気管支反応性亢進	1 (0.3)	0
咳嗽	1 (0.3)	2 (0.7)
呼吸困難	0	1 (0.3)
労作性呼吸困難	1 (0.3)	0
間質性肺疾患	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)		
口腔咽頭痛	2 (0.7)	1 (0.3)
湿性咳嗽	0	1 (0.3)
肺塞栓症	1 (0.3)	0
副鼻腔うっ血	1 (0.3)	1 (0.3)
咽喉刺激感	0	1 (0.3)
皮膚および皮下組織障害	12 (4.1)	10 (3.4)
ざ瘡	4 (1.4)	2 (0.7)
脱毛症	0	2 (0.7)
皮膚炎	1 (0.3)	0
斑状出血	0	1 (0.3)
寝汗	0	1 (0.3)
乾癬	4 (1.4)	1 (0.3)
発疹	1 (0.3)	2 (0.7)
酒さ	1 (0.3)	1 (0.3)
皮膚病変	1 (0.3)	0
血管障害	2 (0.7)	4 (1.4)
高血圧	1 (0.3)	3 (1.0)
低血圧	1 (0.3)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.6.2

Treatment-Emergent Adverse Events with Reasonably Possibly of Being Related to Study Drug per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term - Long Term
(Safety Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 290) (PYs = 292.8) Events (E/100 PYs)	UPA 30 mg QD (N = 308) (PYs = 296.2) Events (E/100 PYs)
血管障害 (Cont.)		
表在性血栓性静脈炎	0	1 (0.3)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

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
腎結石症	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: SCOLIOSIS	19[redacted]
OTHER: CHICKEN POX	19
OTHER: ALLERGIC RHINITIS	19
OTHER: BACK PAIN	19
ALCOHOLISM: HISTORY OF ALCOHOLISM	19
DEPRESSION: CONTROLLED	19
OTHER: ANXIETY	19
OTHER: JOINT PAIN	19
OTHER: PLAQUE PSORIASIS	19
OTHER: RIGHT HAND PAIN	19
HYPERLIPIDEMIA: DYSLIPIDEMIA	20
OTHER: GENERALIZED MUSCLE WEAKNESS	20
OTHER: POSTMENOPAUSAL	20
OTHER: FATIGUE	20
OTHER: BILATERAL UPPER EXTREMITY WEAKNESS	20
OTHER: BENIGN LIPOMA RIGHT ABDOMEN	20
OTHER: BENIGN LIPOMA RIGHT THIGH	20
OTHER: DIFFICULTY SLEEPING	20
OTHER: MEMORY LOSS	20
CARDIAC ARRHYTHMIA: BRADYCARDIA	20
HYPERTENSION	20
OBESITY	20
NEPHROLITHIASIS	20
OTHER: HISTORY OF KERATOTIC LESIONS	20
OTHER: TROCHANTERIC BURSITIS RIGHT HIP	20
PNEUMONIA: LEGIONELLA PNEUMONIA	20
SLEEP APNEA	20
OTHER: ALOPECIA (NON-SCARRING)	20
OTHER: LEFT KNEE PAIN	20
OTHER: HISTORY OF ELEVATED LIVER FUNCTION TESTS OCCASIONAL	20
ANGINA	20[redacted]

OTHER: CYST RIGHT AXILLARY	20[redacted]
OTHER: OSTEOPENIA	20[redacted]
OTHER: SLIPPED DISCS	20[redacted]
OSTEOARTHRITIS: SPINE, BILATERAL KNEES	20[redacted]
OTHER: CELLULITIS OF RIGHT HAND	20[redacted]
OTHER: LEFT ARM PAIN	20[redacted]
OTHER: LEFT ELBOW FRACTURE	20[redacted]
HYPOTHYROIDISM	20[redacted]
OTHER: ENLARGED THYROID	20[redacted]
OTHER: GOITER	20[redacted]

Prior Procedures	Procedure Year
SURGERY: BENIGN LIPOMA RIGHT ABDOMEN EXCISION	20[redacted]
SURGERY: BENIGN LIPOMA RIGHT THIGH EXCISION	20[redacted]
SURGERY: OPEN REDUCTION INTERNAL FIXATION LEFT ELBOW	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	More than 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 392	223

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 19[redacted]
CLOBETASOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
FENOFIBRATE	48 mg	QD	Y-M: 20[redacted]
ATENOLOL	50 mg	QD	Y-M: 20[redacted]
TRAZODONE	100 mg	OTHER: QHS PRN	Y-M: 20[redacted]
BUSPIRONE	30 mg	BID	Y-M: 20[redacted]
LAMOTRIGINE	200 mg	BID	Y-M: 20[redacted] / -221
VENLAFAXINE	300 mg	QD	Y-M: 20[redacted] / -

INFLIXIMAB	3 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted] / -221
PRAZOSIN	1 mg	QD	Y-M: 20[redacted]-[redacted] / -162
NAPROXEN	440 mg	OTHER: QHS	Y-M: 20[redacted]-[redacted] / -131
NAPROXEN	440 mg	PRN	Y-M: 20[redacted]-[redacted] / -101
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted]-[redacted] / -101

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
FENOFIBRATE	48 mg	QD	Y-M: 20[redacted]	ONGOING
ATENOLOL	50 mg	QD	Y-M: 20[redacted]	ONGOING
TRAZODONE	100 mg	OTHER: QHS PRN	Y-M: 20[redacted]	ONGOING
LAMOTRIGINE	200 mg	BID	Y-M: 20[redacted]-[redacted] / -221	ONGOING
VENLAFAXINE	300 mg	QD	Y-M: 20[redacted]-[redacted] / -221	ONGOING
NAPROXEN	440 mg	OTHER: QHS	Y-M: 20[redacted]-[redacted] / -101	ONGOING
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted]-[redacted] / -43	ONGOING
BUSPIRONE	30 mg	QD	Y-M: 20[redacted]-[redacted] / 201	ONGOING
GABAPENTIN	300 mg	BID	Y-M: 20[redacted]-[redacted] / 265	ONGOING
ACICLOVIR	200 mg	OTHER: 5 TIMES/DAY	Y-M: 20[redacted]-[redacted] / 293	Y-M: 20[redacted]-[redacted] / 297
VICODIN	5/325 mg	BID	Y-M: 20[redacted]-[redacted] / 301	ONGOING
PREGABALIN	75 mg	QD	Y-M: 20[redacted]-[redacted] / 302	ONGOING

Event #2: Serious Adverse Event

Event Description	BILATERAL NEPHROLITHIASIS
Preferred term	腎結石症
AE Onset Date / Rx Day	[redacted]20[redacted] / 288
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 288): Erythrocytes: 3.91 [4.2 - 5.4] mU/L; Hematocrit: 0.35 [0.37 - 0.47] fraction of 1; Hemoglobin: 116 [120 - 160] g/L; Leukocytes: 5 [4.8 - 10.8] 10^9/L; Neutrophils: 1.7 [2 - 7.9] 10^9/L; [redacted]20[redacted] (RX DAY 289): Blood: TRACE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 288): CT OF ABDOMEN/ PELVIS: NON-OBSTRUCTIVE NEPHROLITHIASIS PRESENT. SEVERAL STONES BILATERAL KIDNEYS. LARGEST 10MM IN LEFT KIDNEY, HEMORRHAGIC CYST LEFT KIDNEY; ULTRASOUND OF ABDOMEN/PELVIS: BILATERAL OBSTRUCTING RENAL CALCIFICATIONS, HEMORRHAGIC CYST LEFT KIDNEY

AE Stopped Rx Day	293
Duration of AE	6 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN AT THIS TIME-WAITING FOR MEDICAL RECORDS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の6[redacted]歳女性であり，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，両側腎結石症の事象を発現した。

Event 2 の臨床経過：

関連する病歴は側弯症，水疱瘡，背部痛，アルコール症，不安，コントロール下のうつ病，局面型乾癬，乾癬性関節炎，閉経後，疲労，元喫煙者（1 日 1 箱を 30 年間），睡眠困難，高血圧，肥満，角化性病変の既往，腎結石症，椎間板ヘルニア，変形性関節症（脊椎，両膝関節），右手の蜂巣炎，甲状腺肥大，甲状腺腫，甲状腺機能低下症及び元飲酒者（1 日 4 杯超）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両側腎結石症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，両側腎結石症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，重篤な事象である左側腹部の帯状疱疹（治験責任医師の評価に基づき現在は非重篤）のため，ER を受診した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左腰部（側腹部）痛で同病院に入院した。悪心，嘔吐，下痢，発熱，排尿困難及び頻尿は報告されなかった。検

査が行われ，泌尿器科医による診察が行われた。被験者は腎結石症と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for ABT-494 (Blinded)

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1) Nephrolithiasis (10029148) (Nephrolithiasis (10029148)) [v.21.0] [10029148]

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 ABT-494 (Blinded)

Event of BILATERAL NEPHROLITHIASIS

- Investigator: Unknown at this time -waiting for medical records.

- AbbVie: Event more likely related to pre-existing history of nephrolithiasis. pre-existing obesity and hypertension and additional risk factors.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN/PELVIS:** Non-obstructive nephrolithiasis present. Several stones bilateral kidneys. Largest 10mm in left kidney, hemorrhagic cyst left kidney

[redacted] **20[redacted] HEMATOCRIT:** 34.5 % (normal 37 to 47)

[redacted] **20[redacted] HEMOGLOBIN:** 11.6 G/DL (normal 12 to 16)

[redacted] **20[redacted] NEUTROPHILS ABS:** 1.7 X10**3/MCL (normal 2 to 7.9)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.91 mU/L (normal 4.2 to 5.4)

[redacted] **20[redacted] ULTRASOUND ABDOMEN/PELVIS:** Bilateral obstructing renal calcifications, hemorrhagic cyst left kidney

[redacted] **20[redacted] URINE BLOOD:** Trace

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
変形性関節症	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 30 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: ADENOIDECTOMY	19[redacted]
OTHER: TONSILLITIS	19
OTHER: APPENDICITIS	19
GASTROESOPHAGEAL REFLUX DISEASE	19
OTHER: ACID REFLUX	19
OTHER: HEADACHE OCCASIONAL	19
OTHER: DUODENAL ULCER	19
OTHER: PLAQUE PSORIASIS	19
TUBERCULOSIS: (LATENT) TREATED WITH INH	19
MIGRAINE HEADACHE	19
OSTEOARTHRITIS: BILATERAL HANDS	19
OTHER: OCCASIONAL SINUS INFECTION	19
OTHER: VITAMIN D DEFICIENCY	19
OTHER: SEASONAL ALLERGIES	20
HYPERLIPIDEMIA	20
NEPHROLITHIASIS: KIDNEY STONES	20
HYPERTENSION	20
OTHER: INFARCTION LEFT EYE	20
OTHER: HISTORY OF ELEVATED LIVER FUNCTIONS	20
OTHER: RIGHT EYE CATARACT	20
OTHER: HAIR LOSS	20
OTHER: ONE SHINGLE EPISODE	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	19[redacted]
SURGERY: APPENDECTOMY	19[redacted]
SURGERY: CHOLECYSTECTOMY	19[redacted]
SURGERY: COMPLETE HYSTERECTOMY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 161	161
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 162	[redacted]20[redacted] / 392	231
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	500 mg	QD	Y-M: 197[redacted]
ISONIAZID	300 mg	QD	Y-M: 19[redacted]
CALCIUM	600 mg	QD	Y-M: 19[redacted]
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]
MULTIVITAMIN	1 OTHER: TAB	QD	Y-M: 20[redacted]
LORATADINE	10 mg	QD	Y-M: 20[redacted]
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted]
ETANERCEPT	25 mg	EVERY WEEK	Y-M: 20[redacted]
CELECOXIB	200 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
BISELECT	10/625 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	5000 IU	QD	Y-M: 20[redacted]
BIOTIN	1 OTHER: TAB	BID	Y-M: 20[redacted]
FISH OIL	500 mg	QD	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -133
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -133
ULTRA B	1 OTHER: TAB	QD	Y-M: 20[redacted] / -72

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

end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	500 mg	QD	Y-M: 19[redacted]	Not reported.
CALCIUM	600 mg	QD	Y-M: 19[redacted]	Not reported.
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	Not reported.
MULTIVITAMIN	1 OTHER: TAB	QD	Y-M: 20[redacted]	Not reported.
LORATADINE	10 mg	QD	Y-M: 20[redacted]	Not reported.
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted]	Not reported.
CELECOXIB	200 mg	QD	Y-M: 20[redacted]	Not reported.
BISELECT	10/625 mg	QD	Y-M: 20[redacted]	Not reported.
ERGOCALCIFEROL	5000 IU	QD	Y-M: 20[redacted]	Not reported.
BIOTIN	1 OTHER: TAB	BID	Y-M: 20[redacted]	Not reported.
FISH OIL	500 mg	QD	Y-M: 20[redacted]	Not reported.
ULTRA B	1 OTHER: TAB	QD	Y-M: 20[redacted] / -72	Not reported.

Event #1: Serious Adverse Event

Event Description	KELLGREN LAWRENCE GRADE 4 OSTEOARTHRITIS RIGHT HIP
Preferred term	変形性関節症
AE Onset Date / Rx Day	[redacted]20[redacted] / 294
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 316): RIGHT HIP REPLACEMENT: RIGHT HIP OSTEOARTHRITIS GRADE 4 PROCEDURE RIGHT HIP REPLACEMENT RIGHT HIP OSTEOARTHRITIS RESOLVED

AE Stopped Rx Day	316
Duration of AE	23 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	GRADE 4 HIP OSTEOARTHRITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，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，Kellgren-Lawrence 分類グレード 4 の右股関節の変形性関節症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は局面型乾癬，両手関節の変形性関節症，ビタミン D 欠乏，乾癬性関節炎，子宮全摘術，高血圧，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は Kellgren-Lawrence 分類グレード 4 の右股関節の変形性関節症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，Kellgren-Lawrence 分類グレード 4 の右股関節の変形性関節症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は Kellgren Lawrence 分類グレード 4 の右股関節の変形性関節症（非重篤）を発現した。

本事象により治験薬の投与が休止された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，悪化した右股関節痛に対する右人工股関節置換術のため，入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。合併症はなかった。

The patient's past medications include:

INH for TUBERCULOSIS TREATMENT ([redacted] 19[redacted] - [redacted] 19[redacted])

ENBREL for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

HUMIRA for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

BETAMETHASONE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

CLOBETASOL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

DEPO MEDROL for RIGHT HIP BURSITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

XYLOCAINE for RIGHT HIP PAIN BURSITIS and RIGHT HIP PAIN BURSITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) OA hip (10029875) (Osteoarthritis (10031161)) [v.22.0] [10029875]

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 KELLGREN LAWRENCE GRADE 4 OSTEOARTHRITIS RIGHT HIP

- Investigator: GRADE 4 HIP OSTEOARTHRITIS

- AbbVie: Risk factors include advanced age, obesity (BMI 31.1), and pre-existing psoriatic arthritis.

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
頚椎骨折	X			
腰椎骨折	X			
交通事故	X			
胸椎骨折	X			
外傷性血胸	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	7[redacted]	MALE	WHITE

Medical History	Onset Year
HYPERTENSION	19[redacted]
OTHER: REPAIRED PROSTATE DUE TO HERNIATION	20
OTHER: URINARY RETENTION	20
OTHER: IRRITABLE BOWEL SYNDROME	20
OTHER: SEASONAL ALLERGIES	20
CORONARY ARTERY DISEASE: CAD	20
OTHER: ISOLATED GRANULOMAS OF LEFT LOBE	20
OTHER: JUXTAARTICULAR BONE FORMATION	20
OTHER: RT SHOULDER PAIN	20
OTHER: PLAQUE PSORIASIS	20
OTHER: PSORIATIC NAIL DYSTROPHY	20
OTHER: REFLUX ESOPHAGITIS	20
OTHER: LUMBAR RADICULOPATHY	20
SLEEP APNEA	20

Prior Procedures	Procedure Year
SURGERY: CHOLECYSTECOMY- GALLBLADDER REMOVAL	20[redacted]
SURGERY: CHOLEYSTITIS	20[redacted]
SURGERY: HERNIA	20[redacted]
SURGERY: RIGHT 2ND TOE FUSION	20[redacted]
SURGERY: RIGHT GREAT TOE FUSION	20[redacted]
SURGERY: CATARACT SURGERY	20[redacted]
SURGERY: CATARACTS	20[redacted]
SURGERY: INGUINAL HERNIA	20[redacted]
SURGERY: UPPER SCOPIC HERNIORRHAPHY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 166	166
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 167	[redacted]20[redacted] / 390	224
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 391	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METHOTREXATE	25 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted] / -276
NAPROXEN	220 mg	PRN	Y-M: 20[redacted] / -200
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -198
TRIAMCINOLONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -107
DIPHENHYDRAMINE	25 mg	PRN	Y-M: 20[redacted] / -91

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-	Stop Year-Month /

			Month / RX Day	RX Day
NAPROXEN	220 mg	PRN	Y-M: 20[redacted] / - 200	Not reported.
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / - 198	Not reported.
DIPHENHYDRAMINE	25 mg	PRN	Y-M: 20[redacted] / - 91	Not reported.
HYDROCORTISONE	1 OTHER: APPLICATION	OTHER: SMALL APPLICATION TO CORNER OF EYE ONCE DAILY	Y-M: 20[redacted] / 1	Not reported.
ZOLPIDEM	5 mg	QD	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 530
FLUCONAZOLE	50 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / 167	Not reported.
NEUTROGENA T/GEL DAILY 2 IN 1	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 463
BENZONATATE	200 mg	TID	Y-M: 20[redacted] / 211	Not reported.
OSELTAMIVIR	75 mg	BID	Y-M: 20[redacted] / 211	Not reported.
VITEYES	250/2.5/0.5 mg	BID	Y-M: 20[redacted] / 285	Not reported.
DOCUSATE	200 mg	BID	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 467
CALCIUM GLUCONATE	1 g	QD	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 470
EPINEPHRINE	2.5/0.5 mg	OTHER: EVERY 4 HOURS PRN	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 470
FENTANYL	75 OTHER: MCG	QD	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 470
FUROSEMIDE	40/4ML mg	QD	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 470
GLUCOSE	50 %	QD	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 470

INSULIN	100 OTHER: UNITS/1000ML	QD	Y-M: 20[redacted]-20[redacted] / 460 Y-M: 20[redacted]- [redacted] / 470
IPRATROPIUM	0.5/2.5 mg	OTHER: EVERY 4HOURS PRN	Y-M: 20[redacted]-20[redacted] / 460 Y-M: 20[redacted]- [redacted] / 470
LENOLTEC WITH CODEINE NO 1	300/30 mg	OTHER: EVERY 4 HOURS PRN	Y-M: 20[redacted]-20[redacted] / 460 Y-M: 20[redacted]- [redacted] / 470
ONDANSETRON	4 mg	QD	Y-M: 20[redacted]-20[redacted] / 460 Y-M: 20[redacted]- [redacted] / 470
PARACETAMOL	650 mg	OTHER: EVERY 6 HOURS PRN	Y-M: 20[redacted]-20[redacted] / 460 Y-M: 20[redacted]- [redacted] / 470
PROCET	325/5 mg	OTHER: EVERY 6 HOURS PRN	Y-M: 20[redacted]-20[redacted] / 460 Y-M: 20[redacted]- [redacted] / 470
SALBUTAMOL	2.5/0.5 mg	OTHER: EVERY 4 HOURS PRN	Y-M: 20[redacted]-20[redacted] / 460 Y-M: 20[redacted]- [redacted] / 470
CALCIUM GLUCONATE	500 mg	TID	Y-M: 20[redacted]-20[redacted] / 460 Y-M: 20[redacted]- [redacted] / 477
PARACETAMOL	975 mg	OTHER: EVERY 12 HOURS PRN	Y-M: 20[redacted]-20[redacted] / 460 Y-M: 20[redacted]- [redacted] / 497
BACITRACIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-20[redacted] / 461 Y-M: 20[redacted]- [redacted] / 474
LIDOCAINE	1 OTHER: PATCH	QD	Y-M: 20[redacted]-[redacted] / 470 Not reported.
ZOLPIDEM	5 mg	OTHER: QHS	Y-M: 20[redacted]-[redacted] / 470 Not reported.
GABAPENTIN	300 mg	TID	Y-M: 20[redacted]-20[redacted] / 470 Y-M: 20[redacted]- [redacted] / 474
PARACETAMOL	325 mg	TID	Y-M: 20[redacted]-20[redacted] / 470 Y-M: 20[redacted]- [redacted] / 474
BACLOFEN	10 mg	TID	Y-M: 20[redacted]-20[redacted] / 470 Y-M: 20[redacted]- [redacted] / 496
MACROGOL 3350	17 g	QD	Y-M: 20[redacted]-20[redacted] / 470 Y-M: 20[redacted]- [redacted] / 497

Event #1: Serious Adverse Event

Event Description	MOTOR VEHICLE ACCIDENT, CERVICAL SPINE FRACTURE, THORACIC SPINE FRACTURE
Preferred term	頚椎骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 460
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 460): Hemoglobin: 133 [120 - 160] g/L; Potassium: 5.8 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 461): Erythrocytes: 3.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 123 [120 - 160] g/L; Potassium: 4.9 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 462): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 98 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 463): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 99 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 464): Erythrocytes: 2.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 91 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 465): Erythrocytes: 2.7 [4.2 - 5.9] 10^12/L; Hemoglobin: 83 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 466): Erythrocytes: 2.6 [4.2 - 5.9] 10^12/L; Hemoglobin: 82 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 467): Hemoglobin: 89 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 468): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 97 [120 - 160] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 460): CT FACE W/O CONTRAST: UNREMARKABLE CT OF FACE; CT SCAN ABDOMEN AND PELVIS: NO ACUTE INTRA-ABDOMINAL OR PELVIC ABNORMALITIES. DEGENERATIVE CHANGES PRESENT THOUGHT THE LUMBAR SPINE. MULTIPLE CALCIFIED GRANULOMAS IN THE SPLEEN; CT SCAN CHEST, ABDOMEN, PELVIS, THORACIS AND LUMBAR SPINE: NON DISPLACED LINERAR FRACTURE THOUGHT THE BILATERAL PEDICLES OF L3; CT SCAN HEAD/BRAIN: NO ACUTE INTRACRANIAL ABNORMALITIES. CEREBRAL AND CEREBELLER VOLUME LOSS AND PERIVENTRICULAR WHITE MATTER MICROANGIOPATHY; CT SCAN THORAX/ CHEST: FRACTURE DISLOCATION OF T7 VERTEBRAL BODY POSTERIOR DISPLACEMENT AND COMPRESSION OF SPINAL CANAL. AOS TYPE C. LARGE PREVERTEBRAL HEMATOMA NOTES. LARGE RIGHT PLEURAL EFFUSIONN/HEMOTHORAX AND HYPOVENTIL; CT THORACIC SPINE: COMPLETE POSTERIOR TRANSLATION OF T7 AND T8. AOS TYPE C. LARGE RIGHT HEMOTHORAX. STRETCHING OF THE AZYGOUS VEIN AT THE FRACTURE SITE; CTA NECK: UNREMARKABLE CTA OF THE NECK; MRI CERVICAL SPINE: NO ACUTE FRACTURE OF CERVICAL SPINE. MODERATE TO SEVERE CERVICAL SPONDYLOSIS MOST PROMINENT AT THE LEVEL OF C3-C4 AND C4-C5 AND MILD TO MODERATE NARROWING OF NUURAL FORAMINA AT THE LEVER OF C3-C4 AND; MRI LUMBAR: NEGATIVE MRI FOR ACUTE LUMBAR VERTEBRAE FRACTURE OR DISLOCATION. MODERATE LOWER LUMBAR SPONDYLOSIS WITH INTERVERTEBRAL DISC DERANGEMENT PREDOMINATLY AT L3-L4 L4-L5, AND L5 TO S1. RESULTING IN MILD SPI; MRI THORACIC SPINE: BACKGROUND OF DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS, TRANSLATION ROTATION FRACTURE OF T6/7 WITH ANTERIOR

AE Stopped Rx Day	470
Duration of AE	11 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MOTOR VEHICLE ACCIDENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #2: Serious Adverse Event

Event Description	NON DISPLACED FRACTURE OF BILATERAL PEDICLES OF L3
Preferred term	腰椎骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 460
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 460): Hemoglobin: 133 [120 - 160] g/L; Potassium: 5.8 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 461): Erythrocytes: 3.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 123 [120 - 160] g/L; Potassium: 4.9 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 462): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 98 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 463): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 99 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 464): Erythrocytes: 2.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 91 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 465): Erythrocytes: 2.7 [4.2 - 5.9] 10^12/L; Hemoglobin: 83 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 466): Erythrocytes: 2.6 [4.2 - 5.9] 10^12/L; Hemoglobin: 82 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 467): Hemoglobin: 89 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 468): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 97 [120 - 160] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 460): CT FACE W/O CONTRAST: UNREMARKABLE CT OF FACE; CT SCAN ABDOMEN AND PELVIS: NO ACUTE INTRA-ABDOMINAL OR PELVIC ABNORMALITIES. DEGENERATIVE CHANGES PRESENT THOUGHT THE LUMBAR SPINE. MULTIPLE CALCIFIED GRANULOMAS IN THE SPLEEN; CT SCAN CHEST, ABDOMEN, PELVIS, THORACIS AND LUMBAR SPINE: NON DISPLACED LINERAR FRACTURE THOUGHT THE BILATERAL PEDICLES OF L3; CT SCAN HEAD/BRAIN: NO ACUTE INTRACRANIAL ABNORMALITIES. CEREBRAL AND CEREBELLER VOLUME LOSS AND PERIVENTRICULAR WHITE MATTER MICROANGIOPATHY; CT SCAN THORAX/ CHEST: FRACTURE DISLOCATION OF T7 VERTEBRAL BODY POSTERIOR DISPLACEMENT AND COMPRESSION OF SPINAL CANAL. AOS TYPE C. LARGE PREVERTEBRAL HEMATOMA NOTES. LARGE RIGHT PLEURAL EFFUSIONN/HEMOTHORAX AND HYPOVENTIL; CT THORACIC SPINE: COMPLETE POSTERIOR TRANSLATION OF T7 AND T8. AOS TYPE C. LARGE RIGHT HEMOTHORAX. STRETCHING OF THE AZYGOUS VEIN AT THE FRACTURE SITE; CTA NECK: UNREMARKABLE CTA OF THE NECK; MRI CERVICAL SPINE: NO ACUTE FRACTURE OF CERVICAL SPINE. MODERATE TO SEVERE CERVICAL SPONDYLOSIS MOST PROMINENT AT THE LEVEL OF C3-C4 AND C4-C5 AND MILD TO MODERATE NARROWING OF NUURAL FORAMINA AT THE LEVER OF C3-C4 AND; MRI LUMBAR: NEGATIVE MRI FOR ACUTE LUMBAR VERTEBRAE FRACTURE OR DISLOCATION. MODERATE LOWER LUMBAR SPONDYLOSIS WITH INTERVERTEBRAL DISC DERANGEMENT PREDOMINATLY AT L3-L4 L4-L5, AND L5 TO S1. RESULTING IN MILD SPI; MRI THORACIC SPINE: BACKGROUND OF DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS, TRANSLATION ROTATION FRACTURE OF T6/7 WITH ANTERIOR

AE Stopped Rx Day	470
Duration of AE	11 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MOTOR VEHICLE ACCIDENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #3: Serious Adverse Event

Event Description	MOTOR VEHICLE ACCIDENT, CERVICAL SPINE FRACTURE, THORACIC SPINE FRACTURE
Preferred term	交通事故
AE Onset Date / Rx Day	[redacted]20[redacted] / 460
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 460): Hemoglobin: 133 [120 - 160] g/L; Potassium: 5.8 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 461): Erythrocytes: 3.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 123 [120 - 160] g/L; Potassium: 4.9 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 462): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 98 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 463): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 99 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 464): Erythrocytes: 2.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 91 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 465): Erythrocytes: 2.7 [4.2 - 5.9] 10^12/L; Hemoglobin: 83 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 466): Erythrocytes: 2.6 [4.2 - 5.9] 10^12/L; Hemoglobin: 82 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 467): Hemoglobin: 89 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 468): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 97 [120 - 160] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 460): CT FACE W/O CONTRAST: UNREMARKABLE CT OF FACE; CT SCAN ABDOMEN AND PELVIS: NO ACUTE INTRA-ABDOMINAL OR PELVIC ABNORMALITIES. DEGENERATIVE CHANGES PRESENT THOUGHT THE LUMBAR SPINE. MULTIPLE CALCIFIED GRANULOMAS IN THE SPLEEN; CT SCAN CHEST, ABDOMEN, PELVIS, THORACIS AND LUMBAR SPINE: NON DISPLACED LINERAR FRACTURE THOUGHT THE BILATERAL PEDICLES OF L3; CT SCAN HEAD/BRAIN: NO ACUTE INTRACRANIAL ABNORMALITIES. CEREBRAL AND CEREBELLER VOLUME LOSS AND PERIVENTRICULAR WHITE MATTER MICROANGIOPATHY; CT SCAN THORAX/ CHEST: FRACTURE DISLOCATION OF T7 VERTEBRAL BODY POSTERIOR DISPLACEMENT AND COMPRESSION OF SPINAL CANAL. AOS TYPE C. LARGE PREVERTEBRAL HEMATOMA NOTES. LARGE RIGHT PLEURAL EFFUSIONN/HEMOTHORAX AND HYPOVENTIL; CT THORACIC SPINE: COMPLETE POSTERIOR TRANSLATION OF T7 AND T8. AOS TYPE C. LARGE RIGHT HEMOTHORAX. STRETCHING OF THE AZYGOUS VEIN AT THE FRACTURE SITE; CTA NECK: UNREMARKABLE CTA OF THE NECK; MRI CERVICAL SPINE: NO ACUTE FRACTURE OF CERVICAL SPINE. MODERATE TO SEVERE CERVICAL SPONDYLOSIS MOST PROMINENT AT THE LEVEL OF C3-C4 AND C4-C5 AND MILD TO MODERATE NARROWING OF NUURAL FORAMINA AT THE LEVER OF C3-C4 AND; MRI LUMBAR: NEGATIVE MRI FOR ACUTE LUMBAR VERTEBRAE FRACTURE OR DISLOCATION. MODERATE LOWER LUMBAR SPONDYLOSIS WITH INTERVERTEBRAL DISC DERANGEMENT PREDOMINATLY AT L3-L4 L4-L5, AND L5 TO S1. RESULTING IN MILD SPI; MRI THORACIC SPINE: BACKGROUND OF DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS, TRANSLATION ROTATION FRACTURE OF T6/7 WITH ANTERIOR

AE Stopped Rx Day	470
Duration of AE	11 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MOTOR VEHICLE ACCIDENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #4: Serious Adverse Event

Event Description	MOTOR VEHICLE ACCIDENT, CERVICAL SPINE FRACTURE, THORACIC SPINE FRACTURE
Preferred term	胸椎骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 460
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 460): Hemoglobin: 133 [120 - 160] g/L; Potassium: 5.8 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 461): Erythrocytes: 3.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 123 [120 - 160] g/L; Potassium: 4.9 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 462): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 98 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 463): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 99 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 464): Erythrocytes: 2.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 91 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 465): Erythrocytes: 2.7 [4.2 - 5.9] 10^12/L; Hemoglobin: 83 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 466): Erythrocytes: 2.6 [4.2 - 5.9] 10^12/L; Hemoglobin: 82 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 467): Hemoglobin: 89 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 468): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 97 [120 - 160] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 460): CT FACE W/O CONTRAST: UNREMARKABLE CT OF FACE; CT SCAN ABDOMEN AND PELVIS: NO ACUTE INTRA-ABDOMINAL OR PELVIC ABNORMALITIES. DEGENERATIVE CHANGES PRESENT THOUGHT THE LUMBAR SPINE. MULTIPLE CALCIFIED GRANULOMAS IN THE SPLEEN; CT SCAN CHEST, ABDOMEN, PELVIS, THORACIS AND LUMBAR SPINE: NON DISPLACED LINERAR FRACTURE THOUGHT THE BILATERAL PEDICLES OF L3; CT SCAN HEAD/BRAIN: NO ACUTE INTRACRANIAL ABNORMALITIES. CEREBRAL AND CEREBELLER VOLUME LOSS AND PERIVENTRICULAR WHITE MATTER MICROANGIOPATHY; CT SCAN THORAX/ CHEST: FRACTURE DISLOCATION OF T7 VERTEBRAL BODY POSTERIOR DISPLACEMENT AND COMPRESSION OF SPINAL CANAL. AOS TYPE C. LARGE PREVERTEBRAL HEMATOMA NOTES. LARGE RIGHT PLEURAL EFFUSIONN/HEMOTHORAX AND HYPOVENTIL; CT THORACIC SPINE: COMPLETE POSTERIOR TRANSLATION OF T7 AND T8. AOS TYPE C. LARGE RIGHT HEMOTHORAX. STRETCHING OF THE AZYGOUS VEIN AT THE FRACTURE SITE; CTA NECK: UNREMARKABLE CTA OF THE NECK; MRI CERVICAL SPINE: NO ACUTE FRACTURE OF CERVICAL SPINE. MODERATE TO SEVERE CERVICAL SPONDYLOSIS MOST PROMINENT AT THE LEVEL OF C3-C4 AND C4-C5 AND MILD TO MODERATE NARROWING OF NUURAL FORAMINA AT THE LEVER OF C3-C4 AND; MRI LUMBAR: NEGATIVE MRI FOR ACUTE LUMBAR VERTEBRAE FRACTURE OR DISLOCATION. MODERATE LOWER LUMBAR SPONDYLOSIS WITH INTERVERTEBRAL DISC DERANGEMENT PREDOMINATLY AT L3-L4 L4-L5, AND L5 TO S1. RESULTING IN MILD SPI; MRI THORACIC SPINE: BACKGROUND OF DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS, TRANSLATION ROTATION FRACTURE OF T6/7 WITH ANTERIOR

AE Stopped Rx Day	470
Duration of AE	11 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MOTOR VEHICLE ACCIDENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #5: Serious Adverse Event

Event Description	LARGE HEMOPNEUMOTHORAX
Preferred term	外傷性血胸
AE Onset Date / Rx Day	[redacted]20[redacted] / 460
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 460): Hemoglobin: 133 [120 - 160] g/L; Potassium: 5.8 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 461): Erythrocytes: 3.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 123 [120 - 160] g/L; Potassium: 4.9 [3.5 - 5.1] mmol/L; [redacted]20[redacted] (RX DAY 462): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 98 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 463): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 99 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 464): Erythrocytes: 2.9 [4.2 - 5.9] 10^12/L; Hemoglobin: 91 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 465): Erythrocytes: 2.7 [4.2 - 5.9] 10^12/L; Hemoglobin: 83 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 466): Erythrocytes: 2.6 [4.2 - 5.9] 10^12/L; Hemoglobin: 82 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 467): Hemoglobin: 89 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 468): Erythrocytes: 3.2 [4.2 - 5.9] 10^12/L; Hemoglobin: 97 [120 - 160] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 460): CT FACE W/O CONTRAST: UNREMARKABLE CT OF FACE; CT SCAN ABDOMEN AND PELVIS: NO ACUTE INTRA-ABDOMINAL OR PELVIC ABNORMALITIES. DEGENERATIVE CHANGES PRESENT THOUGHT THE LUMBAR SPINE. MULTIPLE CALCIFIED GRANULOMAS IN THE SPLEEN; CT SCAN CHEST, ABDOMEN, PELVIS, THORACIS AND LUMBAR SPINE: NON DISPLACED LINERAR FRACTURE THOUGHT THE BILATERAL PEDICLES OF L3; CT SCAN HEAD/BRAIN: NO ACUTE INTRACRANIAL ABNORMALITIES. CEREBRAL AND CEREBELLER VOLUME LOSS AND PERIVENTRICULAR WHITE MATTER MICROANGIOPATHY; CT SCAN THORAX/ CHEST: FRACTURE DISLOCATION OF T7 VERTEBRAL BODY POSTERIOR DISPLACEMENT AND COMPRESSION OF SPINAL CANAL. AOS TYPE C. LARGE PREVERTEBRAL HEMATOMA NOTES. LARGE RIGHT PLEURAL EFFUSIONN/HEMOTHORAX AND HYPOVENTIL; CT THORACIC SPINE: COMPLETE POSTERIOR TRANSLATION OF T7 AND T8. AOS TYPE C. LARGE RIGHT HEMOTHORAX. STRETCHING OF THE AZYGOUS VEIN AT THE FRACTURE SITE; CTA NECK: UNREMARKABLE CTA OF THE NECK; MRI CERVICAL SPINE: NO ACUTE FRACTURE OF CERVICAL SPINE. MODERATE TO SEVERE CERVICAL SPONDYLOSIS MOST PROMINENT AT THE LEVEL OF C3-C4 AND C4-C5 AND MILD TO MODERATE NARROWING OF NUURAL FORAMINA AT THE LEVER OF C3-C4 AND; MRI LUMBAR: NEGATIVE MRI FOR ACUTE LUMBAR VERTEBRAE FRACTURE OR DISLOCATION. MODERATE LOWER LUMBAR SPONDYLOSIS WITH INTERVERTEBRAL DISC DERANGEMENT PREDOMINATLY AT L3-L4 L4-L5, AND L5 TO S1. RESULTING IN MILD SPI; MRI THORACIC SPINE: BACKGROUND OF DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS, TRANSLATION ROTATION FRACTURE OF T6/7 WITH ANTERIOR

AE Stopped Rx Day	470
Duration of AE	11 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MOTOR VEHICLE ACCIDENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，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，自動車事故，頚椎骨折，胸椎骨折，大量血気胸及び L3 の両側椎弓根の非転位骨折の事象を発現した。

Event 1～5 の臨床経過：

関連する病歴は乾癬性関節炎，右第 2 足指の融合，右足親指の融合，関節近傍骨形成，腰髄神経根障害及び現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は自動車事故，頚椎骨折，胸椎骨折，大量血気胸及び L3 の両側椎弓根の非転位骨折を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，自動車事故，頚椎骨折，胸椎骨折，大量血気胸及び L3 の両側椎弓根の非転位骨折は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は重度の背部痛で入院した。被験者は自動車事故により頚椎・胸椎を骨折及び血気胸を来していた。20[redacted] 年 [redacted] 月 [redacted] 日，胸腔チューブが留置された。20[redacted] 年 [redacted] 月 [redacted] 日，椎弓根スクリューとロッドによる T5～T11 の後方固定術が行われた。In situ 固定術による後方脊椎補強も行われた。20[redacted] 年 [redacted] 月 [redacted] 日，胸腔チューブが抜去された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，リハビリテーション病院に転院した。

投与された薬剤は，オンダンセトロン，インスリン，リドカイン貼付剤，miralax，ガバペンチン，セレコキシブ，MS コンチン，フェンタニル貼付剤，levaquin，racepinephrine，dextrose，グルコン酸カルシウム，イプラトロピウム吸入剤，albuterol，クリンダマイシン，アセトアミノフェン・ヒドロコドン合剤，アセトアミノフェン・コデイン合剤，アセトアミノフェン及びバシトラシンであった。

Causality for UPADACITINIB (Blinded)

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1) Motor vehicle accident (10028008) (Road traffic accident (10039203)) [v.22.0] [10028008]

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

2) Thoracic vertebral fracture (10049948) (Thoracic vertebral fracture (10049948)) [v.22.0] [10049948]

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

3) Fractured cervical spine (10017279) (Cervical vertebral fracture (10049946)) [v.22.0] [10017279]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

4) Hemopneumothorax (10060632) (Traumatic haemothorax (10074487)) [v.22.0] [10060632]

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

5) Lumbar pedicle fracture (10081606) (Lumbar vertebral fracture (10049947)) [v.22.0] [10081606]

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 MOTOR VEHICLE ACCIDENT, CERVICAL SPINE FRACTURE, THORACIC SPINE FRACTURE

- Investigator: MOTOR VEHICLE ACCIDENT

- AbbVie: EVENT IS MORE LIKELY RELATED TO UNEXPECTED, UNINTENTIONAL MOTOR VEHICLE ACCIDENT.

Event of LARGE HEMOPNEUMOTHORAX

- Investigator: MOTOR VEHICLE ACCIDENT

- AbbVie: EVENT IS MORE LIKELY RELATED TO UNEXPECTED, UNINTENTIONAL MOTOR VEHICLE ACCIDENT.

Event of NON DISPLACED FRACTURE OF BILATERAL PEDICLES OF L3

- Investigator: MOTOR VEHICLE ACCIDENT

- AbbVie: EVENT IS MORE LIKELY RELATED TO UNEXPECTED, UNINTENTIONAL MOTOR VEHICLE ACCIDENT.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** CHEST TUBE REMOVED

[redacted] **20[redacted] CHEST X-RAY:** STATUS POST POSTERIOR FUSION OF THE THORACAL CERCIAL SPINE. LOW LUNG COLUMES DUE TO POOR INSPIRATORY EFFORT WITH MINIMAL BASILAR SUBSEGMENTAL ATELECTASIS

[redacted] **20[redacted] CT FACE W/O CONTRAST:** UNREMARKABLE CT OF FACE

[redacted] **20[redacted] CT SCAN ABDOMEN AND PELVIS:** NO ACUTE INTRA-ABDOMINAL OR PELVIC ABNORMALITIES. DEGENERATIVE CHANGES PRESENT THOUGHT THE LUMBAR SPINE. MULTIPLE CALCIFIED GRANULOMAS IN THE SPLEEN

[redacted] 20[redacted] **CT SCAN CHEST, ABDOMEN, PELVIS, THORACIS AND LUMBAR SPINE:** NON DISPLACED LINERAR FRACTURE THOUGHT THE BILATERAL PEDICLES OF L3

[redacted] 20[redacted] **CT SCAN CHEST, ABDOMEN, PELVIS, THORACIS AND LUMBAR SPINE:** NON DISPLACED LINERAR FRACTURE THOUGHT THE BILATERAL PEDICLES OF L3

[redacted] 20[redacted] **CT SCAN CHEST, ABDOMEN, PELVIS, THORACIS AND LUMBAR SPINE:** NON DISPLACED LINERAR FRACTURE THOUGHT THE BILATERAL PEDICLES OF L3

[redacted] 20[redacted] **CT SCAN HEAD/BRAIN:** NO ACUTE INTRACRANIAL ABNORMALITIES. CEREBRAL AND CEREBELLER VOLUME LOSS AND PERIVENTRICULAR WHITE MATTER MICROANGIOPATHY

[redacted] 20[redacted] **CT SCAN THORAX/CHEST:** FRACTURE DISLOCATION OF T7 VERTEBRAL BODY POSTERIOR DISPLACEMENT AND COMPRESSION OF SPINAL CANAL. AOS TYPE C. LARGE PREVERTEBRAL HEMATOMA NOTES. LARGE RIGHT PLEURAL EFFUSIONN/HEMOTHORAX AND HYPOVENTILATION CHANGES IN THE DEPENDENT ASPECT OR RIGHT LUNG.

[redacted] 20[redacted] **CT THORACIC SPINE:** COMPLETE POSTERIOR TRANSLATION OF T7 AND T8. AOS TYPE C. LARGE RIGHT HEMOTHORAX. STRETCHING OF THE AZYGOUS VEIN AT THE FRACTURE SITE

[redacted] 20[redacted] **CT THORAX/CHEST:** FRACTURE DISLOCATION OF T7 VERTEBRAL WITH POSTERIOR DISPLACEMENT. LARGE PREVERTABRAL HEMATOMA. LARGE RIGHT PLEURAL EFFUSION/HEMOTHORAX ANDHYPOVENTILATION CHANGES IN THE DEPENDENT ASPECT OF RIGHT LUNG.

[redacted] 20[redacted] **CTA NECK:** UNREMARKABLE CTA OF THE NECK

[redacted] 20[redacted] **HEMOGLOBIN:** 13.3 G/DL (normal 12 to 16)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.8 G/DL (normal 12 to 16)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.1 G/DL (normal 12 to 16)

[redacted] 20[redacted] **HEMOGLOBIN:** 8.2 G/DL (normal 12 to 16)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.7 G/DL (normal 12 to 16)

[redacted] 20[redacted] **MRI CERVICAL SPINE:** NO ACUTE FRACTURE OF CERVICAL SPINE. MODERATE TO SEVERE CERVICAL SPONDYLOSIS MOST PROMINENT AT THE LEVEL OF C3-C4 AND C4-C5 AND MILD TO MODERATE NARROWING OF NUURAL FORAMINA AT THE LEVER OF C3-C4 AND C4-C5 AS DESCRIBED. BULKY CALCIFICATION OF ANTERIOR LONGITUDINAL LIGAMENTS, SUGGESTIVE OF DIFFUSE SKELETAL HYPEROSTOSIS

[redacted] 20[redacted] **MRI LUMBAR:** NEGATIVE MRI FOR ACUTE LUMBAR VERTEBRAE FRACTURE OR DISLOCATION. MODERATE LOWER LUMBAR SPONDYLOSIS WITH INTERVERTEBRAL DISC DERANGEMENT PREDOMINATLY AT L3-L4 L4-L5, AND L5 TO S1. RESULTING IN MILD SPINAL CANAL STENOSIS AND MODERAL BILATERAL NEURAL FORAMINAL NARROWING.

[redacted] 20[redacted] **MRI THORACIC SPINE:** BACKGROUND OF DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS, TRANSLATION ROTATION FRACTURE OF T6/7 WITH ANTERIOR

DISPLACEMENT OF THORACIC SPINE BELOW T7 LEVEL, ASSOCIATED POSTERIOR LONGITUDINAL LIGAMENT DISRUPTION AND INJURIES OF INTERSPINOUS AND SUPRASPINATUS LIGAMENT AT T7/8 THROUGH T9/10. NO EVIDENCE OF DISC PROTRUSTION OR THORACIC SPINAL CORD COMPRESSION/TRANSECTION.

[redacted] **20[redacted] RED BLOOD CELLS:** 3.94 X10**6/MCL (normal 4.2 to 5.9)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.16 X10**6/MCL (normal 4.2 to 5.9)

[redacted] **20[redacted] RED BLOOD CELLS:** 2.88 X10**6/MCL (normal 4.2 to 5.9)

[redacted] **20[redacted] RED BLOOD CELLS:** 2.64 X10**6/MCL (normal 4.2 to 5.9)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.22 X10**6/MCL (normal 4.2 to 5.9)

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
憩室炎	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: IRRITABLE BOWEL SYNDROME	19[redacted]
OTHER: CHRONIC BACK PAIN	19
OTHER: REACTIVE AIRWAY DISEASE	19
CHOLELITHIASIS	19
HEPATITIS: HEPATITIS C	19
HEPATITIS: TREATED HEPITATIS C	20
OTHER: JUXTAARTICULAR BONE FORMATION	20
OTHER: PSORIATIC NAIL DYSTROPHY	20
OTHER: PLAQUE PSORIASIS	20
DEPRESSION: MILD CONTROLLED DEPRESSION	20
HYPERTENSION	20
OTHER: ENDOMETRIOSIS	20
OTHER: SEASONAL ALLERGIES	20
GASTROESOPHAGEAL REFLUX DISEASE	20
OTHER: GASTRITIS	20
OTHER: PIRIFORMIS SYNDROME	20
OTHER: ROTATOR CUFF SUNDROME	20
CORONARY ARTERY DISEASE	20
OTHER: TROCHANTERIC BURSITIS	20
OTHER: SLEEP DISORDER	20
OTHER: HALLUX RIGIDUS	20
OTHER: OSTEOPENIA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CHOLECYSTECTOMY	19[redacted]
SURGERY: HYSTERECTOMY	20[redacted]
SURGERY: CARDIAC CATH	20[redacted]
SURGERY: LEFT GREAT TOE SURGERY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 298	130

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
PEGINTERFERON	180 OTHER: MCG	EVERY WEEK	Y-M: 19[redacted]
RIBAVIRIN	100 mg	QID	Y-M: 19[redacted]
PARACETAMOL	625 mg	BID	Y-M: 20[redacted]
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]
IBUPROFEN	200 mg	PRN	Y-M: 20[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
CYCLOBENZAPRINE	10 mg	QD	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	325 mg	QD	Y-M: 20[redacted]
ROSUVASTATIN	10 mg	QD	Y-M: 20[redacted]
CERTOLIZUMAB PEGOL	200 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]
MULTIVITAMIN	1 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
CALCIUM WITH VITAMIN D	600-800 OTHER: MG/IU	QD	Y-M: 20[redacted] / -358
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -94

ESCITALOPRAM	10 mg	QD	Y-M: 20[redacted] / -65

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	625 mg	BID	Y-M: 20[redacted]	ONGOING
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]	ONGOING
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]	ONGOING
IBUPROFEN	200 mg	PRN	Y-M: 20[redacted]	ONGOING
CYCLOBENZAPRINE	10 mg	QD	Y-M: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	325 mg	QD	Y-M: 20[redacted]	ONGOING
ROSUVASTATIN	10 mg	QD	Y-M: 20[redacted]	ONGOING
MULTIVITAMIN	1 mg	QD	Y-M: 20[redacted]	ONGOING
CALCIUM WITH VITAMIN D	600-800 OTHER: MG/IU	QD	Y-M: 20[redacted] / -358	ONGOING
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -94	ONGOING
ESCITALOPRAM	10 mg	QD	Y-M: 20[redacted] / -65	ONGOING
COMBIVENT	20/100 OTHER: MCG	BID	Y-M: 20[redacted] / 136	Y-M: 20[redacted] / 148
SODIUM CHLORIDE	1 %	PRN	Y-M: 20[redacted] / 136	Y-M: 20[redacted] / 148
KETOROLAC	30 mg	QD	Y-M: 20[redacted] / 299	Y-M: 20[redacted] / 299
MORPHINE	6 mg	QD	Y-M: 20[redacted] / 299	Y-M: 20[redacted] / 299
LEVOFLOXACIN	750 mg	QD	Y-M: 20[redacted] / 299	Y-M: 20[redacted] / 301
METRONIDAZOLE	500 mg	QD	Y-M: 20[redacted] / 299	Y-M: 20[redacted] / 301
LEVOFLOXACIN	750 mg	QD	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 311
METRONIDAZOLE	500 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 311
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 324	Y-M: 20[redacted] / 334
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 324	Y-M: 20[redacted] / 334

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

Event Description	DIVERTICULITS

Preferred term	憩室炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 299 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 299): CT ABD PELVIS: ACUTE DIVERTICULITIS OF THE MID DESCENDING COLON; TEMPERATURE OF 101.9: TEMPERATURE OBTAINED DURING EMERGENCY TRIAGE. VITALS TAKEN AT 19:56	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳女性であり，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，グレード 3 の憩室炎の事象を発現した。

Event 2 の臨床経過：

関連する病歴は過敏性腸症候群，胆嚢切除，胆石症，C 型肝炎，子宮内膜症，高血圧，胃炎，胃食道逆流性疾患，現喫煙者（1 日 0.5 箱を 20 年間）及び少量の現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は憩室炎を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腹痛及び発熱で入院した。CT スキャンにより憩室炎が認められ，抗生物質が投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，メトロニダゾール，toradol，モルヒネ，フラジール，レボフロキサシン及び levaquin であった。

The patient's past medications include:

HUMIRA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Diverticulitis (10013538) (Diverticulitis (10013538)) [v.22.0] [10013538]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of DIVERTICULITIS

- Investigator: Not applicable.

- AbbVie: Risk factors include obesity, age, and current smoking status.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN PELVIS:** Acute diverticulitis of the mild ascending colon.

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
上気道感染	X			X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	5[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
DIABETES MELLITUS: TYPE II	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]

Prior Procedures	Procedure Year
SURGERY: T4 AND T5 FRACTURE REPAIR	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 393	[redacted]20[redacted] / 553	161

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
PARACETAMOL	650 mg	PRN	Y-M: 19[redacted]
NAPROXEN	220 mg	QD	Y-M: 20[redacted]
RANITIDINE	75 mg	PRN	Y-M: 20[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -357
METFORMIN	1500 mg	QD	Y-M: 20[redacted] / -103

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	650 mg	PRN	Y-M: 19[redacted]	ONGOING
NAPROXEN	220 mg	QD	Y-M: 20[redacted]	ONGOING
RANITIDINE	75 mg	PRN	Y-M: 20[redacted]	ONGOING
METFORMIN	1500 mg	QD	Y-M: 20[redacted] / -103	ONGOING
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted] / 37	ONGOING
AUGMENTIN	875/125 mg	BID	Y-M: 20[redacted] / 450	Y-M: 20[redacted] / 455
CHERACOL	100-10 OTHER: MG/ML	OTHER: 4-6 HOURS AS NEEDED	Y-M: 20[redacted] / 450	Y-M: 20[redacted] / 455

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	UPPER RESPIRATORY INFECTION
Preferred term	上気道感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 450
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted](RX DAY 450): CHEST X-RAY: NO ACUTE PULMONARY DISEASE.

AE Stopped Rx Day	455
Duration of AE	6 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，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，上気道感染の事象を発現した。

Event 1 の臨床経過：

関連する病歴は局面型乾癬，乾癬性関節炎，糖尿病，胃食道逆流性疾患，元喫煙者（1 日 1 箱を 33 年間）及び非飲酒者であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は上気道感染を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，上気道感染は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は息切れのため救急治療室（ER）を受診した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，biotussin AC 及びオーグメンチンであった。

Causality for ABT-494 (Blinded)

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1) Upper respiratory infection (10046300) (Upper respiratory tract infection (10046306)) [v.22.0] [10046300]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of UPPER RESPIRATORY INFECTION

- Investigator: Not Applicable

- AbbVie: Event is common in the general population.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** No acute pulmonary disease

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
一過性全健忘	X			
冠動脈狭窄	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: UTERINE PROLAPSE	19[redacted]
HYPERTENSION	20
OTHER: HYPERCHOLESTEROLEMIA	20
OTHER: SEASONAL ALLERGIES	20
OTHER: PLAQUE PSORIASIS	20
OTHER: ACTINIC KERATOSIS	20
CANCER: SQUAMOUS CELL CARCINOMA IN SITU	20
OTHER: LACUNAR STROKE	20
OTHER: ENTHESOPATHY	20
OTHER: INSOMNIA	20
OTHER: JOINT PAIN	20

Prior Procedures	Procedure Year
SURGERY: HERNIA REPAIR	19[redacted]
SURGERY: HYSTERECTOMY	19
SURGERY: ELECTRODESSICATION AND CURETTAGE	20
SURGERY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 161	161

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / -281
APREMILAST	30 mg	QD	Y-M: 20[redacted] / -181
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -138
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -138
TRAMADOL	50 mg	QD	Y-M: 20[redacted] / -138
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -50
VARICELLA ZOSTER VACCINE	0.65 mL	OTHER: ONCE	Y-M: 20[redacted] / -50
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted] / -35
LISINOPRIL	20 mg	QD	Y-M: 20[redacted] / -35

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / -281	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -138	ONGOING
TRAMADOL	50 mg	QD	Y-M: 20[redacted] / -138	ONGOING
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -138	Y-M: 20[redacted] / 122
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted] / -35	ONGOING
LISINOPRIL	20 mg	QD	Y-M: 20[redacted] / -35	Y-M: 20[redacted] / 88
CEFTRIAXONE	1 g	OTHER: ONCE	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 88
LABETALOL	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 88
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 88
CEFUROXIME	500 mg	BID	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 93
INFLUENZA VACCINE	0.5 mL	OTHER: ONCE	Y-M: 20[redacted] / 90	Y-M: 20[redacted] / 90
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 91	ONGOING
METOPROLOL	25 mg	BID	Y-M: 20[redacted] / 101	ONGOING
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 162
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / 184	ONGOING

Event #1: Serious Adverse Event

Event Description TRANSIENT GLOBAL AMNESIA

Preferred term 一過性全健忘

AE Onset Date / Rx Day [redacted]20[redacted] / 88

Age at AE Onset 6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 88): URINE NPTST142-URINE CULTURE: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 88): CHEST X-RAY: NO EVIDENCE OF ACTIVE CHEST DISEASE; CT HEAD OR BRAIN WITH OUT CONTRAST: CT IMAGING REVEALS NO EVIDENCE OF INTRACRANIAL HEMORRHAGE OR STROKE, SHE DOES HAVE AN OLD LACUNAR STROKE.; EKG: NORMAL AXIS, NORMAL INTERVALS, NO ACUTE ST OR T WAVE CHANGES, NORMAL SINUS RHYTHM AT 77 BPM; MRI BRAIN WITH OUT CONTRAST: NO ACUTE INTRACRANIAL ABNORMALITIES IDENTIFIED

AE Stopped Rx Day 91

Duration of AE 4 DAYS

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	URINARY TRACT INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Study Specific Adverse Events of Interest, Positively Adjudicated Events

Event Description	CORONARY STENOSIS
Preferred term	冠動脈狭窄
AE Onset Date / Rx Day	[redacted]20[redacted] / 129
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 129): ECHOCARDIOGRAM: EJECTION FRACTION OF 55%, MILD AS WITH MILD TO MODERATE AI, AND MITRAL VALVE CALCIFICATION WITH MODERATE MITRAL REGURITATION; [redacted]20[redacted] (RX DAY 162): BILATERAL CAROTID DOPPLER DUPLEX ULTRASOUND: NO HEMODYNAMICALLY SIGNIFICANT STENOSISIDENTIFIED. FLOW IN BOTH VERTEBRAL ARTERIES IS ANTEGRADE TOWARD THE BRAIN; CARDIAC CATHETERIZATION: 80% LEFT MAIN AS WELL AS A 70% LESION OF THE RIGHT CORONARY ARTERY. EJECTION FRACTION WAS 60-70%; CT CHEST/THORAX WITHOUT CONTRAST: EXTENSIVE CORONARY ARTERY CALCIFICATION ARE PRESENT. THE THORACIC AORTA AND SUPRARENAL ABDOMINAL AORTA ARE NORMAL. CALCIFICATION INVOLVING THE THORACIC AORTA. SOME SCARRING IN THE APICES. LINEAR ATELE; [redacted]20[redacted] (RX DAY 163): CORONARY ARTERY BYPASS GRAFTING X3: LEFT INTERNAL MAMMARY ARTERY TO THE LAD, SAPHENOUS VEIN BYPASS GRAFTING TO THE OBTUSE MARGINAL, SAPHENOUS VEIN BYPASS GRAFTING TO THE RIGHT POSTERIOR DECENDING ARTERY; EKG 12 LEAD: NORMAL SINUS RYTHM, LOW VOLTAGE QRS, INFERIOR-POSTERIOR INFARCT, POSSIBLE ACUTE, T WAVE ABNORMALITY, CONSIDER LATERAL ISCHEMIA, ACUTE MI/STEMI, CONSIDER RIGHT VENTRICULAR INVOLVEMENT IN ACUTE INFERIOR; TRANSESOPHAGEAL ECHOCARDIOGRAPHY: MILD MITRAL REGURGITATION, LV SYSTOLIC FUNCTION IS GOOD,NO EVIDENCE OF INTERATRIAL SHUNTING; [redacted]20[redacted] (RX DAY 164): EKG 12 LEAD: NORMAL SINUS RHYTHM, INFERIOR INFARCT, AGE UNDETERMINED

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUBJECTS MEDICAL HISTORY OF HTN AND HYPERCHOLESTEREMIA AND FAMILY HISTORY OF CARDIAC ISSUES
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，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，一過性全健忘の事象を発現した。

Event 1 の臨床経過：

関連する病歴は子宮脱，高血圧，元喫煙者及び現飲酒者（2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は一過性全健忘を発現した。

被験者は，20[redacted] 年 [redacted] 月 [redacted] 日に発現した記憶喪失，錯乱，浮動性めまいなどの精神状態変化のため，救急科を受診した。被験者は混乱しており，勤め先から帰宅したことを覚えておらず，車を運転して帰ってきたのかどうかもわからなかった。また，自分の病状も思い出すことができなかった。被験者は来院したことも覚えていなかったが，自宅の車庫前の通路や，車に乗っていたという事実など，断片的なことは覚えていた。誰が運転して救急科に連れてきてくれたのかは覚えていなかった。来院時に尿路感染及び高血圧が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は経過観察のため入院した。NIH 脳卒中重症度評価スケールはゼロであった。CT スキャン画像により脳卒中の徴候は認められなかったが，陳旧性ラクナ脳卒中が見つかった。さらなる検査で尿路感染（非重篤な事象と判断された）が明らかとなり，それが精神状態変化の原因であると考えられた。投与された薬剤は，セフトリアキソンであった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，メトプロロール酒石酸塩，アスピリン，ラベタロール，ヒドロキシジン塩酸塩，セフトリアキソン及びセフロキシムであった。

Causality for ABT-494 (Blinded)

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1) Transient global amnesia (10044380) (Transient global amnesia (10044380)) [v.22.0] [10044380]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of TRANSIENT GLOBAL AMNESIA

- Investigator: Urinary tract infection

- AbbVie: Event is more likely related to urinary tract infection diagnosed on the same day.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** No evidence of active chest disease

[redacted] **20[redacted] CT HEAD OR BRAIN WITHOUT CONTRAST:** No evidence of intracranial hemorrhage or stroke; old lacunar stroke

[redacted] **20[redacted] EKG:** Normal axis, normal intervals, no acute ST or T wave changes, normal sinus rhythm at 77 bpm

[redacted] **20[redacted] MRI BRAIN WITHOUT CONTRAST:** No acute intracranial abnormalities identified

[redacted] **20[redacted] URINE CULTURE:** Culture-No growth.
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，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，冠動脈狭窄の事象を発現した。

Event 2 の臨床経過：

関連する病歴は高コレステロール血症，高血圧，局面型乾癬，元タバコ使用者，乾癬性関節炎，現飲酒者（2 杯未満），心筋梗塞の家族歴（双子の姉妹が 30 代で心筋梗塞を発症），糖尿病及び CAD 家族歴（父親），CAD 及び心カテーテルの家族歴（姉妹）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は冠動脈狭窄を発現した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，収縮期駆出性雑音（非重篤）があった。

20[redacted] 年 [redacted] 月 [redacted] 日，本事象の諸症状が出現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は安静時及び労作時の不安定狭心症を発現し，入院した。症状は心筋虚血と一致していた。ECG や心臓バイオマーカーの検査は行われなかった。本事象に対する血行再建術が行われた。治験薬の投与は本事象により 20[redacted] 年 [redacted] 月 [redacted] 日に中止された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

病院の退院時サマリー：本被験者は著明なアテローム硬化性冠動脈疾患及び弁正常の狭心症（クラス 4）を有する 6[redacted] 歳の女性であった。被験者は両腕のしびれ感と顎への放散を伴う胸部圧迫感を来した。確かな家族歴（双子の姉妹が 30 代で心筋梗塞を発症し，父親も心臓発作を起こした）があったことから，被験者はカテーテル検査のため当院に直接搬送された。直近の負荷試験で労作時に 3 mm の水平型 ST 低下が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はそのまま当院に入院となり，診断のための左心カテーテル検査を受けた。検査の結果，左主幹動脈に 80%の狭窄，右冠動脈に 70%の狭窄が認められた。駆出率は 60%～70%であった。経食道心エコー検査で重大な弁膜症は認められず，軽度の僧帽弁逆流症及び軽度の大動脈弁閉鎖不全症が認められただけであり，介入は不要であった。

20[redacted] 年 [redacted] 月 [redacted] 日，左内胸動脈から LAD にかけての CABG（3 ヵ所），伏在静脈の鈍縁枝へのバイパス移植術，伏在静脈の右下行後動脈へのバイパス移植術，房室への一時的ペーシングワイヤー挿入，大伏在静脈の内視鏡下静脈採取を行った。被験者はこれらの手術に十分持ちこたえた。術後当初，被験者は不安及び頻呼吸でウィーニングに耐えることができなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者が頻呼吸及び高血圧を伴って容易に覚醒したため，TSB（Vt 250cc）を行った。呼吸数は 20～25 であった。被験者は覚醒しており，会話可能で，椅子に起き上がった。被験者は両腕が動かせないと訴えたが，感覚は失われていなかった。酸素投与は不要であった。反射神経はすべて無傷で，頚部痛や背部痛を訴えることなく立ち上がることができ，楽に呼吸ができた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はアテローム性冠動脈閉塞性疾患による狭心症と診断され，退院した。退院時に創傷ケアと食事に関する指示が出された。

投与された薬剤は nitrostat であった。

Causality for ABT-494 (Blinded)

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1) Coronary artery stenosis (10011089) (Coronary artery stenosis (10011089)) [v.21.0] [10011089]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of CORONARY STENOSIS

- Investigator: Subject's medical history of HTN and hypercholesterolemia and family history of cardiac issues.

- AbbVie: Risk factors include pre-existing hypertension, hypercholesterolemia and strong family history of coronary heart disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] %IMM GRAN:** 1.2 % (normal 0.00 to 0.4)

[redacted] **20[redacted] 12 LEAD EKG:** Normal sinus rhythm, inferior infarct, age undetermined

[redacted] **20[redacted] 12 LEAD EKG:** Normal sinus rhythm, low voltage QRS, inferior-posterior infarct, possible acute, t wave abnormality, consider lateral ischemia, acute mi/stemi, consider right ventricular involvement in acute inferior infarct.

[redacted] **20[redacted] ABS IMM GRAN:** 0.10 K/uL (normal 0.00 to 0.03)

[redacted] **20[redacted] ALT:** 17 IU/L (normal 14 to 54)

[redacted] **20[redacted] AST:** 27 IU/L (normal 15 to 41)

[redacted] **20[redacted] BLOOD GLUCOSE:** 126 mg/dL (normal 70 to 110)

Unknown date BLOOD GLUCOSE: 131 mg/dL (normal 70 to 110)

[redacted] **20[redacted] BLOOD PRESSURE:** 160/80

[redacted] **20[redacted] BODY TEMPERATURE:** 97.3 F

[redacted] **20[redacted] BUN:** 14 MMOL/L (normal 4 to 20)

[redacted] **20[redacted] CALCIUM:** 9.1 mg/dL (normal 8.4 to 10.2)

[redacted] **20[redacted] CALCIUM:** 7.4 mg/dL (normal 8.4 to 10.2)

[redacted] **20[redacted] CALCIUM:** 7.8 mg/dL (normal 8.4 to 10.2)

Unknown date CAROTID ULTRASOUND: No significant carotid lesions

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

[redacted] **20[redacted] CHEST X-RAY:** Postoperative CABG - 2 views: Cardiac silhouette is mildly prominent but improved. Small pleural effusion on the left also appears improved. Atelectasis infiltrate within the left lung base appears improved. Interstitial prominence within the lungs noted bilaterally, improved.

[redacted] **20[redacted] CHLORIDE:** 97 MMOL/L (normal 101 to 111)

[redacted] **20[redacted] CO2:** 28 MMOL/L (normal 22 to 32)

[redacted] **20[redacted] CO2:** 21 MMOL/L (normal 22 to 32)

[redacted] **20[redacted] CREATININE:** 0.9 mg/dL (normal 0.4 to 1.2)

[redacted] **20[redacted] CT CHEST/THORAX:** 1. The heart is not enlarged. Extensive coronary artery calcifications are present. 2. The thoracic aorta and suprarenal abdominal aorta are normal caliber. 3. Calcification involving the thoracic aorta as described above. 4. There is some scarring in the apices. 5. There are areas of 1ine21r atelectasis or scar in moder21te portions of the right upper lobe and left lower lobe. 6. No acute infiltrate, lung mass, or pleural effusion is appreciated.

[redacted] **20[redacted] CT CHEST/THORAX WITHOUT CONTRAST:** Extensive coronary artery calcification are present. The thoracic aorta and suprarenal abdominal aorta are normal. Calcification involving the thoracic aorta. Some scarring in the apices. Linear atelectasis or scar in moderate portions of the right upper lobe and left lobe.

[redacted] **20[redacted] CULTURE:** Scant growth normal upper respiratory flora; no respiratory pathogens

[redacted] **20[redacted] D-DIMER:** 1.52 FEU (normal >0.51)

[redacted] **20[redacted] ECHOCARDIOGRAM:** Ejection fraction of 55%, mild to moderate AI, and mitral valve calcification with moderate mitral regurgitation.

[redacted] **20[redacted] ECHOCARDIOGRAM:** EF 55%, mild AS with mild to moderate AI, mitral valve calcification with moderate MR

[redacted] **20[redacted] FIBRINOGEN:** 127 mg/dL (normal 163 to 493)

[redacted] **20[redacted] GFR:** 56.4 mL/min/1.73m2 (normal >60.0)

[redacted] **20[redacted] GRAM STAIN TRACHEA/ETT/ASPIRATE:** Rare WBC's seen; no organism observed

[redacted] **20[redacted] HEMATOCRIT:** 24.3 % (normal 35.0 to 47.0)

[redacted] **20[redacted] HGB:** 8.4 No units

[redacted] **20[redacted] HGB:** 11.9 G/DL (normal 11.3 to 15.8)

[redacted] **20[redacted] INR:** 1.5 No units

[redacted] **20**[redacted] **INR:** 0.9 No units

[redacted] **20**[redacted] **LYMPH:** 15.0 % (normal 5.0 to 12.0)

[redacted] **20**[redacted] **MAGNESIUM:** 2.0 mg/dL (normal 1.8 to 2.5)

[redacted] **20**[redacted] **MAGNESIUM:** 1.8 mg/dL (normal 1.8 to 2.5)

[redacted] **20**[redacted] **MCHC:** 33.1 G/DL (normal 32 to 36.6)

[redacted] **20**[redacted] **MCV:** 102.9 FL (normal 81.6 to 97.5)

[redacted] **20**[redacted] **NUCLEATED RBC:** 0.4 No units (normal 0.0 to 0.2)

[redacted] **20**[redacted] **O2 SATURATION:** 100 %

[redacted] **20**[redacted] **O2 SATURATION:** 99.4 %

[redacted] **20**[redacted] **PCO2:** 32 mm/hg (normal 35.0 to 45.0)

[redacted] **20**[redacted] **PCO2:** 29.8 mm/hg (normal 35.0 to 45.0)

[redacted] **20**[redacted] **PH:** 7.471 No units (normal 7.30 to 7.450)

[redacted] **20**[redacted] **PH:** 7.484 No units (normal 7.30 to 7.450)

[redacted] **20**[redacted] **PH:** 7.499 No units (normal 7.30 to 7.450)

[redacted] **20**[redacted] **PHOSPORUS:** 1.8 mg/dL (normal 2.4 to 4.7)

[redacted] **20**[redacted] **PLATELET:** 364 k/ul (normal 130 to 400)

[redacted] **20**[redacted] **PO2:** 87.1 mm/hg (normal 75.0 to 100.0)

[redacted] **20**[redacted] **PO2:** 282.4 mm/hg (normal 75.0 to 100.0)

[redacted] **20**[redacted] **POTASSIUM:** 3.8 MMOL/L (normal 3.2 to 5.0)

[redacted] **20**[redacted] **PROTEIN:** 4.7 G/DL (normal 6.1 to 7.9)

[redacted] **20**[redacted] **PROTIME:** 17.1 SEC (normal 8.0 to 11.9)

[redacted] **20**[redacted] **PROTIME:** 9.6 SEC (normal 8.0 to 11.9)

[redacted] **20**[redacted] **PTT:** 30.9 SEC (normal 25.4 to 37.3)

[redacted] **20**[redacted] **PTT:** 30.1 SEC (normal 25.4 to 37.3)

[redacted] **20**[redacted] **PULSE:** 75

[redacted] **20**[redacted] **RBC:** 3.49 m/uL (normal 3.88 to 5.29)

[redacted] **20[redacted] RBC:** 2.78 M/ul (normal 3.88 to 5.29)

[redacted] **20[redacted] RESPIRATORY RATE:** 30

[redacted] **20[redacted] SODIUM:** 140 MMOL/L (normal 136 to 144)

Unknown date STRESS TEST: 3mm horizontal ST depression with exercise

[redacted] **20[redacted] THB:** 9.1 G/DL (normal 12.0 to 18.0)

Unknown date TRANSESOPHAGEAL ECHO: No significant valvular disease with only mild mitral regurgitation and mild aortic insufficiency

[redacted] **20[redacted] URINE CULTURE:** No growth

[redacted] **20[redacted] US CAROTID DUPLEX BILATERAL:** 1. No hemodynamically significant stenosis identified. 2. Flow in both vertebral arteries is antegrade towards the brain.

[redacted] **20[redacted] WBC:** 6.3 KU/L (normal 4.0 to 10.8)

[redacted] **20[redacted] WBC:** 8.4 KU/L (normal 4.0 to 10.8)

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
乾癬性関節症	X	X		

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	7[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: TUBAL LIGATION	19[redacted]
OTHER: POST MENOPAUSAL	19[redacted]
OTHER: SHINGLES, OCCURRED ONCE	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
HYPERTENSION	20[redacted]
OTHER: OSTEOPENIA	20[redacted]
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 86	86

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: EVERY 8 WKS	Y-M: 20[redacted]
MELOXICAM	15 mg	QD	Y-M: 20[redacted]
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted]
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -267
UMECLIDINIUM	1 OTHER: PUFF	PRN	Y-M: 20[redacted] / -168

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	ONGOING
MELOXICAM	15 mg	QD	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted]	ONGOING
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -267	ONGOING
UMECLIDINIUM	1 OTHER: PUFF	PRN	Y-M: 20[redacted] / -168	ONGOING
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 90	ONGOING

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

Event Description	WORSENING PSORIATIC ARTHRITIS
Preferred term	乾癬性関節症
AE Onset Date / Rx Day	[redacted]20[redacted] / 86
Age at AE Onset	7[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 90): DOPPLER'S BILATERALLY: NEGATIVE FOR DVT; [redacted]20[redacted] (RX DAY 100): DRAIN FLUID FROM RIGHT LEG: UNKNOWN

AE Stopped Rx Day	90 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PSORIATIC ARTHRITIS
Discontinued Study Drug Due to the Event	YES

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳女性であり，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，乾癬性関節炎悪化の事象を発現した。

Event 1 の臨床経過：

関連する病歴は元喫煙者（1 日 0.5 箱を 24 年間），閉経後，乾癬性関節炎，高血圧，少量の現飲酒者及び尿路感染症（複数回）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は乾癬性関節炎悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，乾癬性関節炎悪化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，疲労，不安定歩行及びこわばり感を伴う両下肢脱力と 3 日間持続している進行性疼痛の新たな発現により，入院した。被験者の説明によると，疼痛は間欠性の「鈍い痛み」と「鋭い痛み」で，体重負荷で悪化し，安静時に軽減した。身体診察所見は，軽度の両膝関節腫脹（紅斑なし），右側ベーカー嚢腫であった。下肢のしびれ感，サドル麻酔，腸失禁，膀胱性尿失禁，背部痛は認められなかった。両側性 DVT や神経障害はなく，臨床検査値にも異常は認められなかった。水分補給が行われ，抗生物質の投与が継続された。また，PCP 及びリウマチ専門医による慎重な経過観察が行われることとなった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，右下肢のドレナージが行われた。

投与された薬剤はトラマドールであった。

The patient's past medications include:

INFLIXIMAB for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Psoriatic arthritis aggravated (10037161) (Psoriatic arthropathy (10037162)) [v.22.0] [10037161]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING PSORIATIC ARTHRITIS

- Investigator: Psoriatic arthritis

- AbbVie: Event is more likely related to pre-existing psoriatic arthritis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] DOPPLER BILATERALLY:** Negative for DVT. Noted right Backer's cyst.

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
精神状態変化	X			
発熱	X	X		

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 30 mg QD	7[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: ANKLE FRACTURE	19[redacted]
OTHER: COLONOSCOPY	20[redacted]
DEPRESSION: CONTROLLED	20[redacted]
SEXUALLY TRANSMITTED DISEASE: GENITAL HERPES II NOT IN PSORIASIS AREA	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
ANEMIA: N/A	20[redacted]
CHOLECYSTITIS	20[redacted]
SLEEP APNEA	20[redacted]
HYPERLIPIDEMIA: CONTROLLED	20[redacted]
DIABETES MELLITUS: TYPE 2	20[redacted]
HYPERTENSION	20[redacted]
OTHER: EDEMA	20[redacted]
OTHER: NEUROPATHY	20[redacted]
OTHER: HIGH GRADE AV BLOCK WITH 2ND DEGREE AVB & TRIFASCICULAR BLOCK	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	19[redacted]
SURGERY: ANKLE FRACTURE REPAIR	19[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]
SURGERY: DUAL PERMANENT PACEMAKER IMPLANT	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 307	139

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted]
VALACICLOVIR	500 mg	PRN	Y-M: 20[redacted]
IRON	324 mg	QD	Y-M: 20[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
PRAVASTATIN	40 mg	QD	Y-M: 20[redacted]
GOLIMUMAB	50 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
COLECALCIFEROL	1000 IU	QD	Y-M: 20[redacted]
CYANOCOBALAMIN	1000 OTHER: MCG	QD	Y-M: 20[redacted]
CALCIUM	1 OTHER: TAB	PRN	Y-M: 20[redacted]
OTHER RESPIRATORY SYSTEM PRODUCTS	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
METFORMIN	850 mg	BID	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]
AMLODIPINE	2.5 mg	BID	Y-M: 20[redacted]
FUROSEMIDE	20 mg	QD	Y-M: 20[redacted]
LISINOPRIL	20 mg	BID	Y-M: 20[redacted]

METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
FISH OIL	1200 mg	BID	Y-M: 20[redacted]
GABAPENTIN	100 mg	BID	Y-M: 20[redacted]
HYDRALAZINE	10 mg	BID	Y-M: 20[redacted]
POTASSIUM	20 mEq	QD	Y-M: 20[redacted]
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted] / -28

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted]	ONGOING
VALACICLOVIR	500 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 309
IRON	324 mg	QD	Y-M: 20[redacted]	ONGOING
PRAVASTATIN	40 mg	QD	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	1000 IU	QD	Y-M: 20[redacted]	ONGOING
CYANOCOBALAMIN	1000 OTHER: MCG	QD	Y-M: 20[redacted]	ONGOING
CALCIUM	1 OTHER: TAB	PRN	Y-M: 20[redacted]	ONGOING
OTHER RESPIRATORY SYSTEM PRODUCTS	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	ONGOING
METFORMIN	850 mg	BID	Y-M: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	ONGOING
FUROSEMIDE	20 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
FISH OIL	1200 mg	BID	Y-M: 20[redacted]	ONGOING
GABAPENTIN	100 mg	BID	Y-M: 20[redacted]	ONGOING
HYDRALAZINE	10 mg	BID	Y-M: 20[redacted]	ONGOING
POTASSIUM	20 mEq	QD	Y-M: 20[redacted]	ONGOING
AMLODIPINE	5 mg	BID	Y-M: 20[redacted] / 65	ONGOING
LOSARTAN	25 mg	QD	Y-M: 20[redacted] / 156	ONGOING
METOPROLOL	50 mg	QD	Y-M: 20[redacted]	ONGOING

ACICLOVIR	700 mg	TID	Y-M: 20[redacted] / [redacted] / 197 - Y-M: 20[redacted] / [redacted] / 306
AMPICILLIN	2000 mg	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / [redacted] / 306 - Y-M: 20[redacted] / [redacted] / 309
CEFEPIME	2 g	BID	Y-M: 20[redacted] / [redacted] / 306 - Y-M: 20[redacted] / [redacted] / 309
VANCOMYCIN	1250 mg	BID	Y-M: 20[redacted] / [redacted] / 306 - Y-M: 20[redacted] / [redacted] / 309
VALACICLOVIR	1 g	TID	Y-M: 20[redacted] / [redacted] / 309 - ONGOING
AMOXI-CLAVULANICO	875 mg	BID	Y-M: 20[redacted] / [redacted] / 309 - Y-M: 20[redacted] / [redacted] / 316
MINOCYCLINE	100 mg	BID	Y-M: 20[redacted] / [redacted] / 309 - Y-M: 20[redacted] / [redacted] / 316

Event #1: Serious Adverse Event

Event Description	ALTERED MENTAL STATUS
Preferred term	精神状態変化
AE Onset Date / Rx Day	[redacted]20[redacted] / 306
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 306): Blood: POS + 1 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Creatinine: 132.6 [61.88 - 114.92] umol/L; [redacted]20[redacted] (RX DAY 307): NPTST014-ARTERIAL BLLOD GAS PO2: 65 [83 - 108] mmHg; NPTST015-ARTERIAL BLOOD GAS PCO2: 30.9 [35 - 48] mmHg; NPTST016-ARTERIAL BLOOD GAS PH: 7.49 [7.35 - 7.45] UNIT NOT REPORTED; NPTST017-ARTERIAL O2 SATURATION: 94.1 [95 - 99] %; NPTST024-BLOOD GAS HEMOGLOBIN: 9.9 [13.5 - 18] g/dL; NPTST025-BLOOD GAS O2 HEMOGLOBIN: 92.1 [94 - 98] %; NPTST081-LACTATE DEHYDROGENASE: 279 [85 - 245] U/L; NPTST083-LACTIC ACID BLOOD LEVEL: 4.2 [0.9 - 1.7] mmol/L; [redacted]20[redacted] (RX DAY 308): NPTST043-CSF LYMPHOCYTE: 34 [40 - 80] %; NPTST044-CSF MONOCYTE: 53 [15 - 45] %; NPTST045-CSF NEUTROPHILS: 13 [0 - 6] %; NPTST046-CSF PROTEIN: 74 [15 - 45] mg/dL; [redacted]20[redacted] (RX DAY 309): Calcium: 1.97 [2.12 - 2.52] mmol/L; Chloride: 112 [98 - 107] mmol/L; Erythrocytes: 3 [4.5 - 6] 10^12/L; Hematocrit: 0.29 [0.4 - 0.52] fraction of 1; Hemoglobin: 96 [135 - 180] g/L; NPTST029-C REACTIVE PROTEIN: 4.9 [0 - 0.3] mg/dL; Protein: 210 [0 - 120] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 306): CT HEAD W/O CONTRAST: NO CT EVIDENCE FOR ACUTE INTRACRANIAL ABNORMALITY; DX CHEST 1 VIEW PORT: NO ACUTE RADIOGRAPHIC ABNORMALITY OF THE CHEST; [redacted]20[redacted] (RX DAY 307): DX CHEST 1 VIEW PORT: AP VIEW OF THE CHEST. CARDIAC SILHOUETTE IS NORMAL IN SIZE. DUAL-LEAD PACEMAKER, WITH STABLE LEAD POSITION. NO DEVELOPING CONSOLIDATION OR PLEURAL FLUID. OSSEOUS STRUCTURES ARE INTACT.; FLUROSCOPIC-GUIDED LUMBAR PUNCTURE: INDICATION: INFECTION SUCCESSFUL FLUOROSCOPIC-GUIDED LUMBAR PUNCTURE

AE Stopped Rx Day	309 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PRESUMED INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	FEVER
Preferred term	発熱
AE Onset Date / Rx Day	[redacted]20[redacted] / 306
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 306): Blood: POS + 1 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Creatinine: 132.6 [61.88 - 114.92] umol/L; [redacted]20[redacted] (RX DAY 307): NPTST014-ARTERIAL BLLOD GAS PO2: 65 [83 - 108] mmHg; NPTST015-ARTERIAL BLOOD GAS PCO2: 30.9 [35 - 48] mmHg; NPTST016-ARTERIAL BLOOD GAS PH: 7.49 [7.35 - 7.45] UNIT NOT REPORTED; NPTST017-ARTERIAL O2 SATURATION: 94.1 [95 - 99] %; NPTST024-BLOOD GAS HEMOGLOBIN: 9.9 [13.5 - 18] g/dL; NPTST025-BLOOD GAS O2 HEMOGLOBIN: 92.1 [94 - 98] %; NPTST081-LACTATE DEHYDROGENASE: 279 [85 - 245] U/L; NPTST083-LACTIC ACID BLOOD LEVEL: 4.2 [0.9 - 1.7] mmol/L; [redacted]20[redacted] (RX DAY 308): NPTST043-CSF LYMPHOCYTE: 34 [40 - 80] %; NPTST044-CSF MONOCYTE: 53 [15 - 45] %; NPTST045-CSF NEUTROPHILS: 13 [0 - 6] %; NPTST046-CSF PROTEIN: 74 [15 - 45] mg/dL; [redacted]20[redacted] (RX DAY 309): Calcium: 1.97 [2.12 - 2.52] mmol/L; Chloride: 112 [98 - 107] mmol/L; Erythrocytes: 3 [4.5 - 6] 10^12/L; Hematocrit: 0.29 [0.4 - 0.52] fraction of 1; Hemoglobin: 96 [135 - 180] g/L; NPTST029-C REACTIVE PROTEIN: 4.9 [0 - 0.3] mg/dL; Protein: 210 [0 - 120] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 306): CT HEAD W/O CONTRAST: NO CT EVIDENCE FOR ACUTE INTRACRANIAL ABNORMALITY; DX CHEST 1 VIEW PORT: NO ACUTE RADIOGRAPHIC ABNORMALITY OF THE CHEST; [redacted]20[redacted] (RX DAY 307): DX CHEST 1 VIEW PORT: AP VIEW OF THE CHEST. CARDIAC SILHOUETTE IS NORMAL IN SIZE. DUAL-LEAD PACEMAKER, WITH STABLE LEAD POSITION. NO DEVELOPING CONSOLIDATION OR PLEURAL FLUID. OSSEOUS STRUCTURES ARE INTACT.; FLUROSCOPIC-GUIDED LUMBAR PUNCTURE: INDICATION: INFECTION SUCCESSFUL FLUOROSCOPIC-GUIDED LUMBAR PUNCTURE

AE Stopped Rx Day	309 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の7[redacted]歳男性であり，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，発熱及び精神状態変化の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は元喫煙者（1 日 2 箱を 28 年間），コントロール下のうつ病，乾癬性関節炎，2 型糖尿病，デュアルチャンバー永久ペースメーカー移植，第 2 度の AVB 及び三束ブロックを伴う高グレードの AV ブロック，並びに少量の現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 月 [redacted] 日，被験者は発熱及び精神状態変化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，発熱及び精神状態変化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は ER を受診し，精神状態変化，原因不明の発熱及び全身脱力のため入院した。血中乳酸値が 4.2 mmol/L（0.9～1.7）に増加しており，敗血症の可能性があった。急性腎障害はメトホルミン及び ACEI の継続的使用に伴う脱水が原因と考えられた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，マキシピーム，ミノサイクリン，アンピシリン，ゾビラックス，valacyclovir，アモキシシリン・クラブラン酸及びバンコマイシンであった。

The patient's past medications include:

ENBREL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SIMPONI for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SECUKINUMAB for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Fever (10016558) (Pyrexia (10037660)) [v.21.0] [10016558]

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

2) Mental status changes (10048294) (Mental status changes (10048294)) [v.21.0] [10048294]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of FEVER

- Investigator: NOT APPLICABLE

- AbbVie: NOT APPLICABLE

Event of ALTERED MENTAL STATUS

- Investigator: PRESUMED INFECTION.

- AbbVie: EVENT IS MORE LIKELY RELATED TO FEVER AND PRESUMED INFECTION.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ARTERIAL BLOOD GAS PO2:** 65 mmHg (normal 83 to 108)

[redacted] **20[redacted] ARTERIAL BLOOD GAS PCO2:** 30.9 mmHg (normal 35.0 to 48.0)

[redacted] **20[redacted] BLOOD GAS HEMOGLOBIN:** 9.9 G/DL (normal 13.5 to 18.0)

[redacted] **20[redacted] BLOOD GAS O2 HEMOGLOBIN:** 92.1 % (normal 94.0 to 98.0)

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 4.9 mg/dL (normal 0.0 to 0.3)

[redacted] **20[redacted] CALCIUM:** 7.9 mg/dL (normal 8.5 to 10.1)

[redacted] **20[redacted] CHLORIDE:** 112 MEQ/L (normal 98 to 107)

[redacted] **20[redacted] CREATININE:** 1.50 mg/dl (normal 0.70 to 1.30)

[redacted] **20[redacted] CSF LYMPHOCYTE:** 34 % (normal 40 to 80)

[redacted] **20[redacted] CSF MONOCYTE:** 53 % (normal 15 to 45)

[redacted] **20[redacted] CSF NEURTOPHILS:** 13 % (normal 0 to 6)

[redacted] **20[redacted] CSF PROTEIN:** 74 mg/dL (normal 15 to 45)

[redacted] **20[redacted] CT HEAD W/O CONTRAST:** NO CT EVIDENCE FOR ACUTE INTRACRANIAL ABNORMALITY

[redacted] **20[redacted] DX CHEST 1 VIEW PORT:** NO ACUTE RADIOGRAPHIC ABNORMALITY OF THE CHEST

[redacted] **20[redacted] DX CHEST 1 VIEW PORT:** AP VIEW OF THE CHEST. CARDIAC SILHOUETTE IS NORMAL IN SIZE. DUAL-LEAD PACEMAKER, WITH STABLE LEAD POSITION. NO DEVELOPING CONSOLIDATION OR PLEURAL FLUID. OSSEOUS STRUCTURES ARE INTACT.

[redacted] **20[redacted] FLUROSCOPIC-GUIDED LUMBAR PUNCTURE:** INDICATION: INFECTION SUCCESSFUL FLUOROSCOPIC-GUIDED LUMBAR PUNCTURE

[redacted] **20[redacted] HEMATOCRIT:** 28.5 % (normal 40.0 to 52.0)

[redacted] **20[redacted] HEMOGLOBIN:** 9.6 G/DL (normal 13.5 to 18.0)

[redacted] **20[redacted] LACTATE DEHYDROGENASE:** 279 U/L (normal 85 to 245)

[redacted] **20[redacted] LACTATE DEHYDROGENASE:** 279 U/L (normal 85 to 245)

[redacted] **20[redacted] LACTIC ACID BLOOD:** 4.2 MMOL/L (normal 0.9 to 1.7)

[redacted] **20[redacted] LACTIC ACID BLOOD LEVEL:** 4.2 MMOL/L (normal 0.9 to 1.7)

[redacted] **20[redacted] PROTEIN:** 21 mg/dL (normal 0 to 12)

[redacted] **20[redacted] RED BLOOD CELLS:** 2.96 M/uL (normal 4.50 to 6.00)

[redacted] **20[redacted] URINE:** POS + 1--negative

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
良性前立腺肥大症	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	5[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: DEVIATED SEPTUM	20[redacted]
OTHER: CHRONIC NECK PAIN	20
HYPOTHYROIDISM	20
OTHER: HYPOGONADISM	20
OTHER: INSOMNIA	20
OTHER: MUSCLE SPASMS	20
OTHER: PLAQUE PSORIASIS	20
OTHER: RIGHT INDEX FINGER LACERATION WOUND REPAIR	20
BENIGN PROSTATIC HYPERPLASIA	20

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	19[redacted]
SURGERY: SINUS SURGERY	19

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MELOXICAM	15 mg	QD	Y-M: 20[redacted]
THYROID	30 mg	QD	Y-M: 20[redacted]
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted]
VICODIN	10/325 mg	QID	Y-M: 20[redacted]-
SECUKINUMAB	150 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]-
TIZANIDINE	15 mg	QD	Y-M: 20[redacted]-
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]- / -268
CIPROFLOXACIN	500MG mg	BID	Y-M: 20[redacted]- / -1

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MELOXICAM	15 mg	QD	Y-M: 20[redacted]	Not reported.
THYROID	30 mg	QD	Y-M: 20[redacted]	Not reported.
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted]	Not reported.
VICODIN	10/325 mg	QID	Y-M: 20[redacted]-	Not reported.
TIZANIDINE	15 mg	QD	Y-M: 20[redacted]-	Not reported.
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]- / -268	Not reported.
CIPROFLOXACIN	500MG mg	BID	Y-M: 20[redacted]- / -1	Not reported.

Event #1: Serious Adverse Event

Event Description WORSENING BENIGN PROSTATIC HYPERTROPHY
Preferred term 良性前立腺肥大症
AE Onset Date / Rx Day [redacted]20[redacted] / 97
Age at AE Onset 5[redacted]
Laboratory Testing
NOT REPORTED
Microbiology
[redacted]20[redacted] (RX DAY 97): OTHER BLADDER STONE NPTST100-PATHOLOGY: NEGATIVE; OTHER

PROSTATE TISSUE NPTST100-PATHOLOGY: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 97): CYSTOSCOPY WITH CLOT EVACUATION AND FULGURATION OF BLEEDER: THE FOLEY CATHETER WAS REMOVED PRIOR TO PREPPING AND THE 24-FRENCH CONTINUOUS FLOW IGLESIAS RESECTOSCOPE SHEATH WAS PLACED THROUGH THE URETHRA INTO THE BLADDER. THE OBTURATOR WAS REMOVED AND THE RESEC

AE Stopped Rx Day	97
Duration of AE	1 DAY
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HISTORY OF BENIGN PROSTATIC HYPERTROPHY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の5[redacted]歳男性であり，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，良性前立腺肥大悪化の事象を発現した。

Event 1 の臨床経過：

関連する病歴は良性前立腺肥大症であった。

20[redacted]年[redacted]月[redacted]日，被験者は良性前立腺肥大悪化を発現した。20[redacted]年[redacted]月[redacted]日，良性前立腺肥大悪化は消失した。

20[redacted]年[redacted]月[redacted]日，被験者は予定されていた経尿道的前立腺切除術のため入院した。膀胱鏡検査時に血栓除去及び膀胱に対する高周波療法が行われた。20[redacted]年[redacted]月[redacted]日，被験者は退院した。

The patient's past medications include:

SECUKINUMAB for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Benign prostatic hypertrophy (10004447) (Benign prostatic hyperplasia (10004446)) [v.20.1] [10004447]

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 ABT-494 (Blinded)

Event of WORSENING BENIGN PROSTATIC HYPERTROPHY

- Investigator: History of benign prostatic hypertrophy.

- AbbVie: Event is pre-existing and is more likely related to subject's age.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CYSTOSCOPY:** The foley catheter was removed prior to prepping and the 24-french continuous flow iglesias resectoscope sheath was placed through the urethra into the bladder. The obturator was removed and the resectoscope was placed through the sheath. Clots were evacuated from the bladder. There were approx. 350 ml of old clots. The resectoscope was removed and the 22-french 3-way foley catheter was placed through the urethra into the bladder.

[redacted] **20[redacted] PATHOLOGY:** Prostate tissue: Negative Bladder stone: Negative

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
心房細動	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	4[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: TONSILLITIS	19[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: TOOTH INFECTION	20[redacted]
TUBERCULOSIS: LATENT	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPOTHYROIDISM	20[redacted]
OTHER: HYPERCHOLESTEROLEMIA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	19[redacted]
SURGERY: ROOT CANAL	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 394	226
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 395	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]-
NAPROXEN	220 mg	QD	Y-M: 20[redacted]-

METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]
ISONIAZID	300 mg	QD	Y-M: 20[redacted]
PYRIDOXINE	25 mg	QD	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: MONTHLY	Y-M: 20[redacted]
LEVOTHYROXINE	50 OTHER: MCG	QD	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
NAPROXEN	220 mg	QD	Y-M: 20[redacted]	Not reported.
LEVOTHYROXINE	50 OTHER: MCG	QD	Y-M: 20[redacted]	Not reported.
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]	Not reported.
SIMVASTATIN	10 mg	QD	Y-M: 20[redacted] / 23	Not reported.
DILTIAZEM	360 mg	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
ADENOSINE	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 24
DILTIAZEM	5/15 OTHER: MG/HR	PRN	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 24
MEPIVACAINE	10 mL	BID	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 51
MEPIVACAINE	7 mL	OTHER: ONCE	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 51
RADIOTHERAPY	UNKNOWN OTHER: UNKNOWN	OTHER: ONCE	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 51

Event #1: Serious Adverse Event

Event Description	ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE
Preferred term	心房細動
AE Onset Date / Rx Day	[redacted]20[redacted] / 23
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 23): NPTST077-INR: 0.94 [0.9 - 1.2] sec; NPTST088-MAGNESIUM: 2.2 [1.6 - 2.6] mg/dL; NPTST111-PROTIME: 10.2 [9.5 - 12.5] sec; NPTST115-PTT: 26.4 [21 - 31] sec; NPTST135-TROPONIN 1: 0.01 [0 - 0.04] ng/mL; NPTST135-TROPONIN 1: 0.06 [0 - 0.04] ng/mL; [redacted]20[redacted] (RX DAY 24): NPTST135-TROPONIN 1: 0.08 [0 - 0.04] ng/mL; NPTST135-TROPONIN 1: 0.05 [0 - 0.04] ng/mL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 23): COMPREHENSIVE 2D, DOPPLER, AND COLOR-FLOW ECHOCARDIOGRAM: ATRIAL FIBRILLATION; ECG 12 LEAD: ECTOPIC ATRIAL TACHYCARDIA, UNIFOCAL; ECG 12 LEAD: SUPRAVENTRICULAR TACHYCARDIA, REPOLARIZATION ABNORMALITY, PROB RATE RELATED; [redacted]20[redacted] (RX DAY 24): COMPREHENSIVE 2D, DOPPLER, AND COLOR-FLOW ECHOCARDIOGRAM: ATRIAL FIBRILLATION; ECG 12 LEAD: SINUS TACHYCARDIA, MINIMAL ST DEPRESSION, BORDERLINE ST ELEVATION, LATERAL LEADS; ECG 12 LEAD: SINUS TACHYCARDIA, MINIMAL ST DEPRESSION, ST ELEVATION, CONSIDER LATERAL INJURY; [redacted]20[redacted] (RX DAY 25): TREADMILL STRESS TEST: UNABLE TO COMPLETE STRESS TEST DUE TO IMMEDIATE SVT AFTER STARTING THE SVT.; [redacted]20[redacted] (RX DAY 51): SVT ABLATION: RADIOFREQUENCY LESION SUMMARY: 16 APPLICATIONS WERE DELIVERED.TOTAL LESION TIME WAS 691 SEC.

AE Stopped Rx Day	51
Duration of AE	29 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳男性であり，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，頻回心室応答を伴う心房細動の事象を発現した。

Event 1 の臨床経過：

関連する病歴は元喫煙者（1 日 1 箱を 15 年間），局面型乾癬，乾癬性関節炎，甲状腺機能低下症及び現在のアルコール摂取（2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は頻回心室応答を伴う心房細動を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，頻拍性心房細動は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は救急車で救急治療室に搬送され，到着前の約 4 時間にわたり，浮動性めまいが徐々に出現したと訴えた。レストランで食事をしに外出し，帰宅したところ，めまいがしたとのことであった。かかりつけ医を受診したところ，救急治療室に搬送された。搬送中，SVT が認められ，救急隊員がアデノシンを 2 回投与した。救急治療室到着時，被験者は意識清明で見当識（4 項目）正常であり，BP 140/84，中等度の不安が認められた。発熱，胸痛，脚の腫脹，腹痛，悪心／嘔吐，及び下痢は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，SVT に対するアブレーションが行われた。高周波通電病変の要約によると，16 回の通電が行われた。通電時間は計 691 秒であった。

薬物使用の病歴はなかった。

投与された薬剤は，アデノシン，ジルチアゼム及びシンバスタチンであった。放射線照射量 17 2 MGY であった。

The patient's past medications include:

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

APREMILAST for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SECUKINUMAB for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

ISONIAZID for LATENT TB ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PYRIDOXINE HCI for INH TOXICITY PROPHYLAXIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Atrial fibrillation with rapid ventricular response (10058331) (Atrial fibrillation (10003658)) [v.21.1] [10058331]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE

- Investigator: Unknown

- AbbVie: EVENT IS MORE LIKELY RELATED TO OBESITY AND PRE-EXISTING PSORIASIS.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] COMPREHENSIVE 2D, DOPPLER, AND COLOR-FLOW ECHOCARDIOGRAM:** ATRIAL FIBRILLATION

[redacted] **20[redacted] COMPREHENSIVE 2D, DOPPLER, AND COLOR-FLOW ECHOCARDIOGRAM:** Left ventricular systolic function is normal. LVEF 60%. mild concentric left ventricular hypertrophy. left atrium is mildly dialated. no significant valvular abnormalities.

[redacted] **20[redacted] ECG 12 LEAD:** SUPRAVENTRICULAR TACHYCARDIA, REPOLARIZATION ABNORMALITY, PROB RATE RELATED

[redacted] **20[redacted] ECG 12 LEAD:** ECTOPIC ATRIAL TACHYCARDIA, UNIFOCAL

[redacted] **20[redacted] ECG 12 LEAD:** SINUS TACHYCARDIA, MINIMAL ST DEPRESSION, BORDERLINE ST ELEVATION, LATERAL LEADS

[redacted] **20[redacted] ECG 12 LEAD:** SINUS TACHYCARDIA, MINIMAL ST DEPRESSION, ST ELEVATION, CONSIDER LATERAL INJURY

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Normal

[redacted] **20[redacted] INR:** 0.94 SEC (normal 0.9 to 1.2)

[redacted] **20[redacted] MAGNESIUM:** 2.20 mg/dL (normal 1.60 to 2.60)

[redacted] **20[redacted] PROTIME:** 10.2 SEC (normal 9.5 to 12.5)

[redacted] **20[redacted] PTT:** 26.4SEC (normal 21 to 31)

[redacted] **TREADMILL STRESS TEST:** UNABLE TO COMPLETE STRESS TEST DUE TO IMMEDIATE SVT AFTER STARTING THE SVT

[redacted] **TROPONIN 1:** 0.01 NG/ML (normal 0 to 0.04)

[redacted] **TROPONIN 1:** 0.06 NG/ML (normal 0 to 0.04)

[redacted] **TROPONIN 1:** 0.08 NG/ML (normal 0 to 0.04)

[redacted] **TROPONIN 1:** 0.05 NG/ML (normal 0 to 0.04)

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
直腸癌	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: CERVICAL DYSPLASIA	19[redacted]
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20
OTHER: PLAQUE PSORIASIS	20
NEPHROLITHIASIS	20
HYPERTENSION	20
OTHER: POSTMENOPAUSAL	20
OTHER: URINARY TRACT INFECTION	20

Prior Procedures	Procedure Year
SURGERY: CAESAREAN DELIVERY	19[redacted]
SURGERY: CAESAREAN DELIVERY	19
SURGERY: CERVICAL CRYOSURGERY	19
SURGERY: DILATION AND CURETTAGE	19
SURGERY: CHOLYCYSTECTOMY	20
SURGERY: LITHOTRIPSY	20

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 94	94

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
NAPROXEN	400 mg	PRN	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
NAPROXEN	400 mg	PRN	Y-M: 20[redacted]	ONGOING
HYDROCORTISONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 32	ONGOING
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted]-[redacted] / 76	Y-M: 20[redacted]-[redacted] / 78
ANTINEOPLASTIC AGENTS	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]-[redacted] / 115	ONGOING

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

Event Description	SQUAMOUS CELL CARCINOMA, KERATINIZING, MODERATELY DIFFERENTIATED, RECTUM
Preferred term	直腸癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 64
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 64): COLONOSCOPY: PER PATHOLOGIST. GRADE II SQUAMOUS CELL CARCINOMA, KERATINIZING, MODERATELY DIFFERENTIATED. STAGE T2N0M0; [redacted]20[redacted] (RX DAY 87): COMPUTERIZED TOMOGRAPHY SCAN OF ABDOMEN AND PELVIS: ANAL CANCER CONFIRMED LIMITED TO RECUM; [redacted]20[redacted] (RX DAY 98): RADIATION: COMPLETED; [redacted]20[redacted] (RX DAY 114): VENOUS PORT PLACEMENT: SUCCESSFUL PLACEMENT

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the	YES

Event
SAE Criteria OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳女性であり，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，角化型及び中分化型直腸扁平上皮癌の事象を発現した。

Event 1 の臨床経過：

関連する病歴は子宮頚部凍結手術，子宮頚部上皮異形成，局面型乾癬，胆嚢切除，高血圧，閉経後，非喫煙者及び少量の現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は角化型及び中分化型直腸扁平上皮癌を発現した。

本事象発現前の 20[redacted] 年 [redacted] 月，被験者は痔核（非重篤な事象）を発現した。

被験者は 20[redacted] 年 [redacted] 月より続いていた直腸出血で来院した。20[redacted] 年 [redacted] 月 [redacted] 日，痔核を伴う直腸出血について調べるため結腸内視鏡検査を行ったところ，肛門癌が見つかった。CT スキャンにより腫瘍は直腸に限局することが確認された。20[redacted] 年 [redacted] 月 [redacted] 日，放射線療法が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，化学療法を開始するための静脈ポートが留置された。20[redacted] 年 [redacted] 月 [redacted] 日，化学療法が開始された。

がんの家族歴の有無は不明であった。

本事象により，この被験者の治験は中止された。

The patient's past medications include:

ADALIMUMAB for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Squamous cell carcinoma of rectum (10066437) (Rectal cancer (10038038)) [v.22.0] [10066437]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of SQUAMOUS CELL CARCINOMA, KERATINIZING, MODERATELY DIFFERENTIATED, RECTUM

- Investigator: Not Applicable.

- AbbVie: WEAK TEMPORAL ASSOCIATION, WITH APPROXIMATELY ONLY 3 MONTHS OF STUDY DRUG EXPOSURE PRIOR TO ONSET OF THE EVENT.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **PATHOLOGY:** Colonoscopy specimens - Per pathologist : Grade II squamous cell carcinoma, Keratinizing, moderately differentiated. Stage T2N0M0

[redacted] **CT SCAN OF ABDOMEN AND PELVIS:** Anal cancer confirmed limited to rectum.

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
心房細動	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 30 mg QD	8[redacted]	MALE	WHITE

Medical History	Onset Year
GASTROESOPHAGEAL REFLUX DISEASE	19[redacted]
HYPERTENSION	19
OTHER: PLAQUE PSORIASIS	19
OTHER: INTERMITTENT PRE TIBIAL EDEMA	20
CHOLELITHIASIS	20
HYPERLIPIDEMIA: NO ADDITIONAL INFORMATION	20
KIDNEY DISORDER: CHRONIC KIDNEY DISEASE STAGE 3	20
OTHER: SCROTAL SWELLING	20
OTHER: LEFT BROKEN ANKLE SECONDARY TO FALL	20
OTHER: BILATERAL PLEURAL EFFUSIONS	20
DIABETES MELLITUS: TYPE II	20
OTHER: CARDIOMEGALLY	20
CORONARY ARTERY DISEASE: NO ADDITIONAL INFORMATION AVAILABLE	20
OTHER: ISCHEMIC MYOPATHY	20
OTHER: ENLARGED PROSTATE	20
OTHER: BIBASILAR ATELECTASIS	20

Prior Procedures	Procedure Year
SURGERY: ABDOMINAL HERNIA REPAIR	19[redacted]
SURGERY: CORONARY ARTERY BYPASS GRAFTING	19[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]
SURGERY: CORONARY ARTERY BYPASS GRAFTING	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 172	172
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 173	[redacted]20[redacted] / 203	31

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 19[redacted]
ETANERCEPT	25 mg	EVERY WEEK	Y-M: 20[redacted]
TOCOPHEROL W/VITAMIN D NOS	1 OTHER: TAB	QD	Y-M: 20[redacted]
VITAMIN B-COMPLEX	1 OTHER: TAB	QD	Y-M: 20[redacted]
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted]
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]
METOPROLOL	25 mg	BID	Y-M: 20[redacted]
ATORVASTATIN	40 mg	QD	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
ISOSORBIDE MONONITRATE	15 mg	BID	Y-M: 20[redacted]
RANOLAZINE	1000 mg	QD	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]-
METFORMIN	500 mg	BID	Y-M: 20[redacted]-
METOLAZONE	2.5 mg	PRN	Y-M: 20[redacted]
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]
BUMETANIDE	1 mg	BID	Y-M: 20[redacted]-
IBUPROFEN	800 mg	QD	Y-M: 20[redacted]- / -57

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-	Stop Year-

			Month / RX Day	Month / RX Day
TOCOPHEROL W/VITAMIN D NOS	1 OTHER: TAB	QD	Y-M: 20[redacted]	ONGOING
VITAMIN B-COMPLEX	1 OTHER: TAB	QD	Y-M: 20[redacted]	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 193
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 193
METOPROLOL	25 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 193
ATORVASTATIN	40 mg	QD	Y-M: 20[redacted]	ONGOING
ISOSORBIDE MONONITRATE	15 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 193
RANOLAZINE	1000 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 193
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted]	ONGOING
APREMILAST	30 mg	BID	Y-M: 20[redacted]	ONGOING
METFORMIN	500 mg	BID	Y-M: 20[redacted]	ONGOING
METOLAZONE	2.5 mg	PRN	Y-M: 20[redacted]	ONGOING
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]	ONGOING
BUMETANIDE	1 mg	BID	Y-M: 20[redacted]	ONGOING
IBUPROFEN	800 mg	QD	Y-M: 20[redacted] / - 57	Y-M: 20[redacted] / 193
DIPHTHERIA VACCINE TOXOID W/PERTUSS	0.5 mL	OTHER: ONCE	Y-M: 20[redacted] / 193	Y-M: 20[redacted] / 193
BUMETANIDE	1 mg	QD	Y-M: 20[redacted] / 193	Y-M: 20[redacted] / 194
ISOSORBIDE MONONITRATE	60 mg	QD	Y-M: 20[redacted] / 193	Y-M: 20[redacted] / 194
MILRINONE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 193	Y-M: 20[redacted] / 194
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 193	Y-M: 20[redacted] / 194
CEFTRIAXONE	1 g	QD	Y-M: 20[redacted] / 193	Y-M: 20[redacted] / 197
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 193	Y-M: 20[redacted] / 197
CHLOROTHIAZIDE	500 mg	QD	Y-M: 20[redacted] / 194	Y-M: 20[redacted] / 194
HEPARIN	5000 IU	OTHER: ONCE	Y-M: 20[redacted] / 194	Y-M: 20[redacted] / 194
LIDOCAINE	5 mL	OTHER: ONCE	Y-M: 20[redacted] / 194	Y-M: 20[redacted] / 194
HEPARIN	25000 IU	QD	Y-M: 20[redacted] / 194	Y-M: 20[redacted] / 196

ALBUMIN HUMAN	12.5 g	OTHER: ONCE	Y-M: 20[redacted] / 195	Y-M: 20[redacted] / 195
APIXABAN	2.5 mg	BID	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 197
CEFUROXIME	500 mg	BID	Y-M: 20[redacted] / 197	Y-M: 20[redacted] / 202

Event #2: Serious Adverse Event

Event Description	ATRIAL FIBRILLATION
Preferred term	心房細動
AE Onset Date / Rx Day	[redacted]20[redacted] / 193
Age at AE Onset	8[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 193): Sodium: 136 [137 - 145] mmol/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 193): CT ABDOMEN AND CT PELVIS WITHOUT CONTRAST: MILD TO MODERATE ASCITES, CIRRHOSIS, BILATERAL COMMON FEMORAL ARTERY SACCULAR ANEURYSMS, MEASURING APPROXIMATELY 5X4.6CM ON THE RIGHT AND 4.2X 4.4 CM ON THE LEFT.; CT CHEST WITHOUT CONTRAST: MODERATE RIGHT AND SMALL LEFT PLEURAL EFFUSIONS. MILD BIBASILAR ATELECTASIS. CARDIOMEGALY. ATHEROSCLRETIC CHANGES OF CORONARY ARTERIES, SUBCLAVIAN ARTERIES AND THORACIC AORTA; CT HEAD WITHOUT CONTRAST: NO ACUTE INTRACRANIAL HEMORRHAGE, MILD ATROPHY, MILD CHRONIC SMALL VESSEL ISCHEMIC CHANGES, FOCAL RIGHT PARIETAL SCALP SOFT TISSUE SWELLING; CT MAXILLOFACIAL/SINUS WITHOUT CONTRAST: NO ACUTE ABNORMALITIES; CT SPINE CERVICAL WITHOUT CONTRAST: NO EVIDENCE OF ACUTE OSSEOUS INJURY, ADVANCED MULTILEVEL DEGENERATIVE CHANGES OF THE CERVICAL SPINE, SMALL RIGHT PLEURAL EFFUSION; EKG STANDARD: ATRIAL FIBRILLATION WITH PREMATURE VENTRICULAR CONTRACTIONS OR ABERRANTLY CONDUCTED COMPLEXES; LEFT AXIS DEVIATION; LEFT BUNDLE BRANCH BLOCK; NONSPECIFIC ST AND T WAVE ABNORMALITY.; XRAY CHEST: SMALL BILATERAL EFFUSION, BIBASILAR AIRSPACE DISEASE; [redacted]20[redacted] (RX DAY 194): US PARACENTESIS: SUCCESSFUL; [redacted]20[redacted] (RX DAY 196): TRANSESOPHAGEAL ECHOCARDIOGRAPHY: MODERATE LV DYSFUNCTION WITH NO INTRACARDIAC THROMBUS AND NO SIGNIFICANT VALVULAR ISSUES

AE Stopped Rx Day	197
Duration of AE	5 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THE SUBJECT'S AGE, HISTORY OF CORONARY ARTERY DISEASE AND DIABETES ARE ALL LIKELY CAUSES.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 8[redacted] 歳男性であり，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，心房細動の事象を発現した。

Event 2 の臨床経過：

関連する病歴は冠動脈バイパス術 2 回，高血圧，第 3 期慢性腎臓病，高脂血症，転倒による左足関節部骨折，2 型糖尿病，心拡大，冠動脈疾患及び虚血性ミオパチーであった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は心房細動を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，心房細動は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は自宅での転倒後，脱力で入院した。被験者は，虚血性心筋症，トロポニン増加，BNP 増加など，複数の医学的問題に対する検査のため，入院した。20[redacted] 年 [redacted] 月 [redacted] 日，心臓除細動が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

病院の退院時サマリーによると，被験者は転倒後，20[redacted] 年 [redacted] 月 [redacted] 日に入院し，心房細動が新たに発現した。S/P TEE で，心臓除細動は成功した。失神は心房細動におそらく関連あるものであった。体重減少及び食欲減退が認められた。栄養補給のため，エンシュアの投与が開始された。原因不明の腹水を伴う肝硬変が認められた。心腎症候群：クレアチニンは改善した。診断：虚血性心筋症，自宅での転倒。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，ヘパリン及びエリキュースであった。

Causality for ABT-494 (Blinded)

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1) Atrial fibrillation (10003658) (Atrial fibrillation (10003658)) [v.21.0] [10003658]

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 ABT-494 (Blinded)

Event of ATRIAL FIBRILLATION

- Investigator: THE SUBJECT'S AGE, HISTORY OF CORONARY ARTERY DISEASE AND DIABETES ARE ALL LIKELY CAUSES.

- AbbVie: EVENT MORE LIKELY RELATED TO AGE, CORONARY ARTERY DISEASE, HYPERTENSION, DIABETES MELLITUS, AND CHRONIC KIDNEY DISEASE STAGE 3.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN AND CT PELVIS WITHOUT CONTRAST:** Mild to moderate ascites, cirrhosis, bilateral common femoral artery saccular aneurysms, measuring approximately 5x4.6cm on the right and 4.2x 4.4 cm on the left.

[redacted] **20[redacted] CT ABDOMEN AND CT PELVIS WITHOUT CONTRAST:** Mild to moderate ascites, cirrhosis, bilateral common femoral artery saccular aneurysms, measuring approximately 5x4.6cm on the right and 4.2x 4.4 cm on the left.

[redacted] **20[redacted] CT CHEST WITHOUT CONTRAST:** Moderate right and small left pleural effusions. Mild bibasilar atelectasis. Cardiomegaly. Atherosclerotic changes of coronary arteries, subclavian arteries and thoracic aorta.

[redacted] **20[redacted] CT HEAD WITHOUT CONTRAST:** No acute intracranial hemorrhage, mild atrophy, mild chronic small vessel ischemic changes, focal right parietal scalp soft tissue swelling.

[redacted] **20[redacted] CT MAXILLOFACIAL/SINUS WITHOUT CONTRAST:** No acute abnormalities

[redacted] **20[redacted] CT SPINE CERVICAL WITHOUT CONTRAST:** No evidence of acute osseous injury, advanced multilevel degenerative changes of the cervical spine, small right pleural effusion.

Unknown date ECHOCARDIOGRAM: Per hospital discharge record: During hospitalization latest echo results: Mild left ventricular hypertrophy. Severe left ventricular systolic dysfunction. The ejection fraction is visually estimated to be 35%. Regional wall motion abnormality is present. Moderate enlargement of the left atrium. Moderate enlargement of the right atrium. Mild mitral valve regurgitation. Mild to moderate tricuspid valve regurgitation. The pulmonary artery pressure is severely increased.

[redacted] **20[redacted] ECHOCARDIOGRAM - TEE:** Moderate LV dysfunction with no intracardiac thrombus and no significant valvular issues.

[redacted] **20[redacted] EKG STANDARD:** Atrial fibrillation with premature ventricular contractions or aberrantly conducted complexes; left axis deviation; anteroseptal infarct, age undetermined; ST&T wave abnormality,

consider lateral ischemia.

[redacted] **20[redacted] EKG STANDARD:** Atrial fibrillation with premature ventricular contractions or aberrantly conducted complexes; left axis deviation; left bundle branch block; nonspecific ST and T wave abnormality.

[redacted] **20[redacted] EKG STANDARD:** Atrial flutter with 3:1 AV conduction, Leftaxis deviation, Non specific intraventricular block, cannot rule out anterior infarct, T wave abnormality, consider lateral ischemia.

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

[redacted] **20[redacted] TRANSESOPHAGEAL ECHOCARDIOGRAPHY:** Moderate LV dysfunction with no intracardiac thrombus and no significant valvular issues.

[redacted] **20[redacted] X-RAY CHEST:** Small bilateral effusion, bibasilar airspace disease.

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
気管支炎	X			X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: AMENORRHEA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: SEBACEOUS CYST REMOVAL SURGERY (RIGHT LEG)	19[redacted]
SURGERY: SEBACEOUS CYST REMOVAL SURGERY (RIGHT HIP)	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 249	81

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PANADEINE CO	ACETAMINOPHEN - 300 CODEINE- 30 mg	PRN	Y-M: 20[redacted]-[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]-[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]-[redacted] / -280

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
PANADEINE CO	ACETAMINOPHEN - 300 CODEINE- 30 mg	PRN	Y-M: 20[redacted]-[redacted]	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]-[redacted]	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]	Y-M: 20[redacted]-[redacted] / 108
AZITHROMYCIN	500 mg	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / 6	Y-M: 20[redacted]-[redacted] / 8
CLINDAMYCIN	600 mg	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / 6	Y-M: 20[redacted]-[redacted] / 8
IPRATROPIUM	500 ug	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / 6	Y-M: 20[redacted]-[redacted] / 8
LACTOBACILLUS ACIDOPHILUS	UNKNOWN OTHER: UNKNOWN	OTHER: DAILY	Y-M: 20[redacted]-[redacted] / 6	Y-M: 20[redacted]-[redacted] / 8
MUPIROCIN	1 OTHER: APPLICATIONS	TID	Y-M: 20[redacted]-[redacted] / 6	Y-M: 20[redacted]-[redacted] / 8
SALBUTAMOL	2.5 mg	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / 6	Y-M: 20[redacted]-[redacted] / 8
AZITHROMYCIN	250 mg	QD	Y-M: 20[redacted]-[redacted] / 8	Y-M: 20[redacted]-[redacted] / 12
BENZONATATE	100 mg	TID	Y-M: 20[redacted]-[redacted] / 8	Y-M: 20[redacted]-[redacted] / 28
IPRATROPIUM	2 OTHER: PUFFS	OTHER: EVERY 6 HOURS	Y-M: 20[redacted]-[redacted] / 8	Y-M: 20[redacted]-[redacted] / 28
SALBUTAMOL	2 OTHER: PUFFS	OTHER: EVERY 6 HOURS	Y-M: 20[redacted]-[redacted] / 8	Y-M: 20[redacted]-[redacted] / 28

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	ACUTE BRONCHITIS
Preferred term	気管支炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 4

Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	29
Duration of AE	26 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	VIRAL VS. BACTERIAL INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者はプエルトリコの 5[redacted] 歳女性であり，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，急性気管支炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は局面型乾癬，乾癬性関節炎，紙巻タバコ喫煙者（1 日 0.5 箱を 40 年）及び少量の現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性気管支炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性気管支炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，24 時間持続している湿性咳嗽，倦怠感及び労作時呼吸困難のため来院した。同日入院し，急性気管支炎と診断され，投薬が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は安定状態で退院した。

投与された薬剤は，proventil HFA，イプラトロピウム臭化物，ムピロシン，tessalon perles，albuterol sulfate nebulization，albuterol，アトロベント，アジスロマイシン及び cleocin phosphate であった。

The patient's past medications include:

HUMIRA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Acute bronchitis (10000687) (Bronchitis (10006451)) [v.21.0] [10000687]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of ACUTE BRONCHITIS

- Investigator: Viral versus bacterial infection

- 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
肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: POST MENOPAUSAL	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
HYPERTENSION	20[redacted]
OTHER: TRANSAMINITIS	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 167	167
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 168	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
APREMILAST	30 mg	QD	Y-M: 20[redacted]
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
NAPROXEN	500 mg	QD	Y-M: 20[redacted]
USTEKINUMAB	45 mg	OTHER: EVERY 12 WEEKS	Y-M: 20[redacted]
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted]
MONASCUS PURPUREUS	300 mg	QD	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
APREMILAST	30 mg	QD	Y-M: 20[redacted]	Not reported.
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]	Not reported.
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	Not reported.
NAPROXEN	500 mg	QD	Y-M: 20[redacted]	Not reported.
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted]	Not reported.
MONASCUS PURPUREUS	300 mg	QD	Y-M: 20[redacted]	Not reported.

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description PNEUMONIA

Preferred term 肺炎

AE Onset Date / Rx Day [redacted]20[redacted] / 177

Age at AE Onset 6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 183): CT ABDOMEN/PELVIS W/O CONTRAST: THERE IS A 2.3 CM CALCIFIED GALLSTONE IN THE GALLBLADDER; [redacted]20[redacted] (RX DAY 184): CT CHEST W/O CONTRAST: THERE IS A SMALL AREA OF ACUTE INFILTRATE INVOLVING THE LEFT UPPER LOBE COMPATIBLE WITH PNEUMONIA; [redacted]20[redacted] (RX DAY 187): CHEST XRAY 1 VIEW: THE CARDIAC SILHOUTTE IS UNREMARKABLE. THE TRACHEA IS MIDLINE. THE LUNGS ARE CLEAR. THERE IS NO EVIDENCE FOR AIRSPACE CONSOLIDATION OR EFFUSION.; [redacted]20[redacted] (RX DAY 191): NUCLEAR GALLUM SCAN: STUDY SHOWS A NORMAL UPTAKE IN THE LIVER AND SPLEEN AND COLON. THERE IS ABNORMALUPTAKE TO SUGGEST ABSCESS FORMATION OR INFFLAMATORY CHANGES.

AE Stopped Rx Day 192

Duration of AE 16 DAYS

Relation to Study Drug by Investigator REASONABLE POSSIBILITY

Investigator Alternative Etiology NOT REPORTED

Discontinued Study Drug Due to the Event NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，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，肺炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は閉経後，局面型乾癬，乾癬性関節炎，非喫煙者及び非飲酒者であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は発熱で入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

STELARA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.22.0] [10035664]

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 PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X RAY:** NORMAL AT SCREENING

[redacted] **20[redacted] CHEST X RAY:** The cardiac silhouette was unremarkable. The trachea is midline. The lungs are clear. There was no evidence for airspace consolidation or effusion.

[redacted] **20[redacted] CT ABDOMEN/PELIVS W/O CONTRAST:** There was a 2.3 cm calcified gallstones in the gallbladder.

[redacted] **20[redacted] CT CHEST W/O CONTRAST:** There was a small area of acute infiltrate involving the left upper lobe compatible with pneumonia.

[redacted] **20[redacted] NUCLEAR GALLUM SCAN:** Study shows a normal uptake in the liver and spleen and colon. There was abnormal uptake to suggest abscess formation or inflammatory changes.

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
不安定狭心症	X			X
血管偽動脈瘤	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 30 mg QD	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
MIGRAINE HEADACHE	19[redacted]
OTHER: INSOMNIA	19
OTHER: ANXIETY	20
OSTEOARTHRITIS: RIGHT KNEE	20
OTHER: LOWER BACK PAIN INTERMITTIENT	20
OBESITY	20
OTHER: PLAQUE PSORIASIS	20
CORONARY ARTERY DISEASE: FOUND ON CARDIO CATHER	20
HYPERLIPIDEMIA: HYPERCHOLESTEROLEMIA, MILD NO MEDS	20
OTHER: CARDIOMEGALY	20
OTHER: ABNORMAL EKG	20
OTHER: POST MENAPAUSAL	20
OTHER: UPPER RESPIRATORY INFECTION	20

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	19[redacted]
SURGERY: BILATERAL CARPAL TUNNEL REPAIR	20
SURGERY: CARDIO CATHETERIZATION	20
SURGERY: HYSTERECTOMY	20

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted] / 1	[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted] / 169	[redacted] / 395	227
ABT-494	30MG	ORAL	QD	[redacted] / 396	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AMITRIPTYLINE	10 mg	QD	Y-M: 20[redacted]
LORAZEPAM	1 mg	QD	Y-M: 20[redacted]
ETANERCEPT	50 OTHER: MG/ML	EVERY WEEK	Y-M: 20[redacted]
APREMILAST	30 mg	QD	Y-M: 20[redacted]
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted]
VICODIN	325/10 mg	QD	Y-M: 20[redacted]
CYCLOBENZAPRINE	10 mg	PRN	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / -141
AUGMENTIN	500 mg	QD	Y-M: 20[redacted] / -26

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AMITRIPTYLINE	10 mg	QD	Y-M: 20[redacted]	Not reported.
LORAZEPAM	1 mg	QD	Y-M: 20[redacted]	Not reported.
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted]	Not reported.
VICODIN	325/10 mg	QD	Y-M: 20[redacted]	Not reported.
CYCLOBENZAPRINE	10 mg	PRN	Y-M: 20[redacted]	Not reported.
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / -141	Y-M: 20[redacted] / 86
IOHEXOL	350 mg	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 82
KETOROLAC	30 mg	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 82
MORPHINE	2 mg	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] /

CARVEDILOL	3.125 mg	QD	Y-M: 20[redacted]82 /	Y-M: 20[redacted]82 /
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted]82 /	Y-M: 20[redacted]83 /
DOCUSATE	50 mg	BID	Y-M: 20[redacted]82 /	Y-M: 20[redacted]83 /
MORPHINE	4 mg	QD	Y-M: 20[redacted]82 /	Y-M: 20[redacted]86 /
NALOXONE	0.4 mg	QD	Y-M: 20[redacted]82 /	Y-M: 20[redacted]86 /
ONDANSETRON	4 mg	QD	Y-M: 20[redacted]82 /	Y-M: 20[redacted]86 /
OXYCODONE	5 mg	QD	Y-M: 20[redacted]82 /	Y-M: 20[redacted]86 /
PARACETAMOL	325 mg	BID	Y-M: 20[redacted]82 /	Y-M: 20[redacted]86 /
SODIUM CHLORIDE	2 mL	QD	Y-M: 20[redacted]82 /	Y-M: 20[redacted]86 /
ENOXAPARIN	100 mg	QD	Y-M: 20[redacted]83 /	Y-M: 20[redacted]85 /
APREMILAST	30 mg	QD	Y-M: 20[redacted]83 /	Y-M: 20[redacted]86 /
ATORVASTATIN	80 mg	QD	Y-M: 20[redacted]83 /	Y-M: 20[redacted]86 /
CLOPIDOGREL	300 mg	BID	Y-M: 20[redacted]85 /	Y-M: 20[redacted]85 /
FENTANYL	100 ug	QD	Y-M: 20[redacted]85 /	Y-M: 20[redacted]85 /
HEPARIN	1000 IU	QD	Y-M: 20[redacted]85 /	Y-M: 20[redacted]85 /
HEPARIN	2000 IU	QD	Y-M: 20[redacted]85 /	Y-M: 20[redacted]85 /
MIDAZOLAM	2 mg	QD	Y-M: 20[redacted]85 /	Y-M: 20[redacted]85 /
SODIUM CHLORIDE	0.9 %	QD	Y-M: 20[redacted]85 /	Y-M: 20[redacted]86 /
TIROFIBAN	12.5/250 OTHER: MG/ML	QD	Y-M: 20[redacted]85 /	Y-M: 20[redacted]86 /
ACETYLSALICYLIC ACID	81 mg	BID	Y-M: 20[redacted]86 /	Not reported.
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted]86 /	Not reported.
ACETYLSALICYLIC ACID	81 mg	BID	Y-M: 20[redacted]86 /	Y-M: 20[redacted]86 /
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted]86 /	Y-M: 20[redacted]86 /
RAMIPRIL	2.5 mg	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] /

ATORVASTATIN	80 mg	QD	Y-M: 20[redacted]-[redacted] 86 /	Y-M: 20[redacted]-[redacted] 86 /
MORPHINE	2 mg	QD	Y-M: 20[redacted]-[redacted] 86 /	Y-M: 20[redacted]-[redacted] 212 /
ACETYLSALICYLIC ACID	162 mg	QD	Y-M: 20[redacted]-[redacted] 87 /	Y-M: 20[redacted]-[redacted] 88 /
			Y-M: 20[redacted]-[redacted] 88	Y-M: 20[redacted]-[redacted] 88

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest, Positively Adjudicated Events

Event Description UNSTABLE ANGINA

Preferred term 不安定狭心症

AE Onset Date / Rx Day [redacted]20[redacted] / 82

Age at AE Onset 4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 82): CHEST X-RAY: MILD COMPENSATED CARDIOMEGALY; CT ANGIOGRAPHY: PROMINENT GOITER WITH SUBSTERNAL MASS COMPONENT; [redacted]20[redacted] (RX DAY 83): THYROID ULTRASOUND: THYROMEGALY WITH HETEROGENEOUS ECHOTEXTURE; [redacted]20[redacted] (RX DAY 85): HEART CATHETERIZATION WITH STENT: MILD TO MODERATE CORONARY ARTERY DISEASE

AE Stopped Rx Day 86

Duration of AE 5 DAYS

Relation to Study Drug by Investigator NO REASONABLE POSSIBILITY

Investigator Alternative Etiology PAST HISTORY OF CARDIAC CATHETERIZATION ON [redacted] 20[redacted] AND A HISTORY OF MILD HYPERCHOLESTEROLEMIA

Discontinued Study Drug Due to the Event NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description PSEUDOANEURYSM OF ARTERY OF LOWER EXTREMITY

Preferred term 血管偽動脈瘤

AE Onset Date / Rx Day [redacted]20[redacted] / 87

Age at AE Onset 4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 89): EMBOLIZATION TRANSCATHETER: UNCOMPLICATED OCCLUSION OF PSEUDOANEURYSM; LOWER EXTREMITY ULTRASOUND: HEMATOMA RIGHT LEG; PELVIS CT:

PARTIALLY THROMBOSED PSEUDOANEURYSM WITH A 4.4 CM NECK EMANATING FROM THE DISTAL RIGHT COMMON FEMORAL ARTERY

AE Stopped Rx Day	92
Duration of AE	6 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COMPLICATIONS FROM THE CARDIAC CATHETERIZATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳女性であり，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，不安定狭心症及び下肢偽動脈瘤の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は不安，病的肥満，乾癬性関節炎，心拡大，冠動脈疾患，高コレステロール血症（軽度，投薬なし），心電図異常，心カテーテル，右冠動脈の 60%狭窄，閉経後，現喫煙者（1 日 1 箱を 27 年間），現飲酒者（2 杯未満）及び本態性高血圧症であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は不安定狭心症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，不安定狭心症は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は下肢偽動脈瘤を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，下肢偽動脈瘤は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸骨下胸痛の急性出現により入院した。肩甲骨内への放散を伴う圧迫感で，発汗はなかった。被験者は医療上の指示に従っていなかった。急性冠動脈症候群の可能性は一連の酵素検査及び心電図により除外された。テレメトリーによるモニタリングが継続され，心カテーテル検査が予定された。20[redacted] 年 [redacted] 月 [redacted] 日，右中央冠動脈近位部にステントを挿入する心カテーテル検査が行われた。軽度から中等度の冠動脈疾患が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，退院後，被験者が咳をすると右鼡径部に急激な痛みが生じ，腫脹と皮下出血を来した。20[redacted] 年 [redacted] 月 [redacted] 日，腫脹の軽快が認められたが，被験者は経過観察及び血管手術の評価のため入院した。骨盤 CT 検査により，右総大腿動脈遠位部を起始部とする部分的に血栓化した偽動脈瘤と，右前内側大腿部の血腫が明らかとなった。被験者は医師による超音波検査を

受け，観察下に置かれた。20[redacted] 年 [redacted] 月 [redacted] 日，画像下で偽動脈瘤の塞栓術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は症状なく臨床的に改善しており，退院した。

投与された薬剤は，エノキサパリンナトリウム，アスピリン，リピトール，ramipril，ketorolac tromethamine，モルヒネ硫酸塩，アセトアミノフェン，ナロキソン，オンダンセトロン，オキシコドン，ヘパリン，ミダゾラム，フェンタニル，モルヒネ，アスピリン，クレストール，アトルバスタチン，カルベジロール，tirofiban 及びクロピドグレルであった。

The patient's past medications include:

ENBREL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

OTEZLA for PSORIATIC ARTHRITIS (20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Unstable angina (10046251) (Angina unstable (10002388)) [v.22.0] [10046251]

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

2) Pseudoaneurysm (10048977) (Vascular pseudoaneurysm (10048975)) [v.22.0] [10048977]

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 UNSTABLE ANGINA

- Investigator: PAST HISTORY OF CARDIAC CATHETERIZATION ON [redacted] 20[redacted] AND A HISTORY OF MILD HYPERCHOLESTEROLEMIA.

- AbbVie: RISK FACTORS INCLUDE, PRE-EXISTING CORONARY ARTERY DISEASE, HYPERLIPIDEMIA, AND CURRENT SMOKER (1 PPD X 27 YRS).

Event of PSEUDO ANEURYSM OF ARTERY OF LOWER EXTREMITY

- Investigator: Complications from the cardiac catheterization

- AbbVie: Event is more likely a complication of recent cardiac catheterization

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD PRESSURE: 111/61 mmHg

[redacted] 20[redacted] CHEST X-RAY: mild compensated cardiomegaly, no pneumothorax

[redacted] 20[redacted] CHOLESTEROL: 226 no unit

[redacted] 20[redacted] CT ANGIOGRAPHY: Prominent goiter with substernal mass component. no evidence of pulmonary embolism

[redacted] 20[redacted] D-DIMER: 0.91 no unit

Unknown date EKG: normal sinus rhythm at 87 bpm, small Q waves in the interior leads which are non diagnostic

Unknown date BODY WEIGHT: 158 KG

[redacted] 20[redacted] HDL: 31.3 no unit

[redacted] 20[redacted] HEART RATE: 78 /min

[redacted] 20[redacted] HEMATOCRIT: 41.9 no unit

[redacted] 20[redacted] HEMOGLOBIN: 13.8 no unit

[redacted] 20[redacted] INR: 1.1 no unit

[redacted] 20[redacted] LDL: 144 no unit

[redacted] 20[redacted] LEFT HEART CATHETERIZATION: Questionable culprit lesion being either the proximal first diagonal artery and/or the proximal right coronary artery; otherwise , mild to moderate 3 vessel coronary disease in a right dominant system. Normal LV systolic function, EF 60%; successful direct PCI bare metal stent of the proximal right coronary artery from 75% with TIMI 3 flow.

[redacted] 20[redacted] LOWER EXTREMITY ULTRASOUND: complex 8.7 x 11.9 x 3.4cm hematoma in the medial thigh; partially thrombosed pseudoaneurysm measuring 3.2 x 2.6 x 2.0 cm with a prominent neck measuring

almost 7mm in diameter. The common femoral artery itself appears to be aneurysmal in the region of the pseudoaneurysm measuring 2.5 x 2.5 x 2.3 cm with mural thrombus.

[redacted] **20[redacted] PELVIS CT:** A 2.7cm partially thrombosed pseudoaneurysm with a 4.4 cm neck emanating from the distal right common femoral artery; 15.9 x 4.7 cm hematoma in the anteromedial right thigh

[redacted] **20[redacted] PLATELET COUNT:** 139 MM**3 (normal 150 to 450)

[redacted] **20[redacted] PROTHROMBIN TIME:** 11.2 no unit

[redacted] **20[redacted] RANDOM GLUCOSE:** 120 mg/dL

[redacted] **20[redacted] RBC:** 4.74 no unit

[redacted] **20[redacted] RBC:** 3.99 X10**3/MM**3 (normal 4.00 to 5.30)

[redacted] **20[redacted] THYROID ULTRASOUND:** thyromegaly with herterogenous echotexture. No evidence of discrete nodule or mass. No evidence of adenopathy

[redacted] **20[redacted] TRIGLYCERIDES:** 252 no unit

[redacted] **20[redacted] TROPONIN I:** less than 0.02 ng/mL

[redacted] **20[redacted] TROPONIN I:** less than 0.02 ng/mL

[redacted] **20[redacted] TSH:** 1.170 no unit

[redacted] **20[redacted] WBC:** 10.6 no unit

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
胃腸炎	X			X
吐血	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: ALLERGY TO BEES ANAPHYLAXIS	NOT REPORTED
DRUG ALLERGIES/REACTIONS: ALLERGY TO ENBREL, MUSCLE CONTRACTIONS	NOT REPORTED
DRUG ALLERGIES/REACTIONS: ALLERGY TO HUMIRA, RASH AND WELTS	NOT REPORTED
DRUG ALLERGIES/REACTIONS: ALLERGY TO IODINE ANAPHYLAXIS	NOT REPORTED
DRUG ALLERGIES/REACTIONS: ALLERGY TO LEFLUNOMIDE, LIVER TOXICITY	NOT REPORTED
DRUG ALLERGIES/REACTIONS: ALLERGY TO LORTAB, GI UPSET	NOT REPORTED
DRUG ALLERGIES/REACTIONS: ALLERGY TO OTEZLA, URI AND NAUSEA AND VOMITING	NOT REPORTED
DRUG ALLERGIES/REACTIONS: ALLERGY TO REMICADE, RASH	NOT REPORTED
OTHER: POST MENOPAUSAL	20[redacted]
OSTEOARTHRITIS: SPINE	20[redacted]
DEPRESSION: SITUATIONAL	20[redacted]
OTHER: ANXIETY	20[redacted]
OTHER: LOWER BACK PAIN	20[redacted]
OTHER: SEASON ALLERGIES	20[redacted]
OTHER: CERVICAL SPONDYLOSIS WITH MYELOPATHY	20[redacted]
PEPTIC ULCER DISEASE: RESOLVED IN 20[redacted]	20[redacted]
OTHER: PLAQUE PSOROSIS	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: POSTMENOPAUSAL OSTEOPOROSIS	20[redacted]
OTHER: SHORTNESS OF BREATH	20[redacted]
OTHER: HISTORY OF RIGHT BUNDLE BRANCH BLOCK	20[redacted]

Prior Procedures	Procedure Year

SURGERY: OVARIAN WEDGE RESECTION WITH HYSTERECTOMY	19[redacted]
SURGERY: RIGHT CARPAL TUNNEL SURGERY	19[redacted]
SURGERY: DISCECTOMY CERVICAL MULTIPLE DISC	20[redacted]
SURGERY: RIGHT ROTARY CUFF REPAIR	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
DULOXETINE	60 mg	QD	Y-M: 20[redacted]
TIZANIDINE	4 mg	BID	Y-M: 20[redacted]
LORATADINE	10 mg	PRN	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: 2 DOSES ONLY	Y-M: 20[redacted]
APREMILAST	10 mg	QD	Y-M: 20[redacted]
ETANERCEPT	50 mg	OTHER: ONE DOSE ONLY	Y-M: 20[redacted]
INFLIXIMAB	5MG/KG mg	OTHER: ONE DOSE	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]
OXYCOCET	1 mg	PRN	Y-M: 20[redacted]
ALENDRONIC ACID	70 mg	EVERY WEEK	Y-M: 20[redacted]
SALBUTAMOL	90 ug	PRN	Y-M: 20[redacted]
LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
DULOXETINE	60 mg	QD	Y-M: 20[redacted]	Not reported.
TIZANIDINE	4 mg	BID	Y-M: 20[redacted]	Not reported.
LORATADINE	10 mg	PRN	Y-M: 20[redacted]	Not reported.
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 450
ALENDRONIC ACID	70 mg	EVERY WEEK	Y-M: 20[redacted]	Not reported.

SALBUTAMOL	90 ug	PRN	Y-M: 20[redacted]	Not reported.
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 453
SUCRALFATE	1 g	BID	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 453
PNEUMOCOCCAL VACCINE	0.5 mL	OTHER: ONCE	Y-M: 20[redacted] / 445	Y-M: 20[redacted] / 445

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description GASTROENTERITIS
Preferred term 胃腸炎
AE Onset Date / Rx Day [redacted]20[redacted] / 441
Age at AE Onset 6[redacted]
Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 446): CT ABDOMINAL-PELVIS WITHOUT CONTRAST: NO DEFINITE FINDING TO EXPLAIN ETIOLOGY OF HEMATEMESIS; [redacted]20[redacted] (RX DAY 447): EGD: GRADE C ESOPHAGITIS , HIATAL HERNIA, NONOBSTRUCTIVE SCHATZKI'S RING AND GASTRITIS; ULTRASOUND RIGHT UPPER QUADRANT: NORMAL RIGHT UPPER QUADRANT ULTRASOUND; X-RAY RIGHT KNEE: DEGENERATIVE OSTEOARTHRITIS NEGATIVE FOR ACUTE INJURY; [redacted]20[redacted] (RX DAY 449): DOPPLER EXTREMITY UPPER VEIN: THROMBOSIS OF THE RIGHT PROXIMAL MID AND DISTAL CEPHALIC VEIN
AE Stopped Rx Day 450
Duration of AE 10 DAYS
Relation to Study Drug by Investigator NO REASONABLE POSSIBILITY
Investigator Alternative Etiology STOMACH VIRUS
Discontinued Study Drug Due to the Event NO
SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description HEMATEMESIS
Preferred term 吐血
AE Onset Date / Rx Day 07JUL2019 / 441
Age at AE Onset 6[redacted]
Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 446): CT ABDOMINAL-PELVIS WITHOUT CONTRAST: NO DEFINITE FINDING TO EXPLAIN ETIOLOGY OF HEMATEMESIS; [redacted]20[redacted] (RX DAY 447): EGD: GRADE C ESOPHAGITIS , HIATAL HERNIA, NONOBSTRUCTIVE SCHATZKI'S RING AND GASTRITIS; ULTRASOUND RIGHT UPPER QUADRANT: NORMAL RIGHT UPPER QUADRANT ULTRASOUND;

X-RAY RIGHT KNEE: DEGENERATIVE OSTEOARTHRITIS NEGATIVE FOR ACUTE INJURY; [redacted]20[redacted] (RX DAY 449): DOPPLER EXTREMITY UPPER VEIN: THROMBOSIS OF THE RIGHT PROXIMAL MID AND DISTAL CEPHALIC VEIN

AE Stopped Rx Day	450
Duration of AE	10 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUBJECT EXPERIENCED GASTROENTERITIS AND HEMATEMESIS RELATED TO FAMILY MEMBERS EXPERIENCING THE SAME
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の6[redacted]歳女性であり，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，吐血及び胃腸炎の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は閉経後，不安，状況因性うつ病，消化性潰瘍疾患，乾癬性関節炎，局面型乾癬，不眠症，元紙巻タバコ喫煙者（1 日 1 箱を 51 年間，2015 年に禁煙）及び禁酒であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted]年[redacted]月[redacted]日，ABT-494 の盲検投与が開始された。

20[redacted]年[redacted]月[redacted]日，被験者は吐血を発現した。20[redacted]年[redacted]月[redacted]日，被験者は胃腸炎を発現した。20[redacted]年[redacted]月[redacted]日，吐血及び胃腸炎は消失した。

20[redacted]年[redacted]月[redacted]日，被験者は 3 日前から発現していた嘔吐，悪心及び下痢のため入院した。被験者と一緒にいた孫（男児）も同じ症状を呈していた。被験者は出血を伴わない嘔吐を複数回繰り返していた。発熱，悪寒及び胸痛はないとのことであった。CT 検査及び超音波検査により異常は認められなかった。食道胃十二指腸内視鏡検査により，グレード C のびらん性食道炎，食道裂孔ヘルニア，非閉塞性 Schatzki 輪及び胃炎が認められた。被験者は胃腸炎及び吐血を来したが，これは家族にも起こった。20[redacted]年[redacted]月[redacted]日，被験者は退院した。

院内記録によると，Protonix の投与も開始された。吐血については，明確な原因は不明であった。

投与された薬剤は，carafate，zofran 及びニューモバックス 23 であった。

The patient's past medications include:

ENBREL for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

HUMIRA for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

OTEZLA for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

REMICADE for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

LEFLUNOMIDE for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

VALACYCLOVIR for SKIN ERUPTION RASH LEFT CHEEK ([redacted] 20[redacted] - [redacted] 20[redacted])

IODINE for UNKNOWN INDICATION

LORTAB for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Hematemesis (10019418) (Haematemesis (10018830)) [v.22.0] [10019418]

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

2) Gastroenteritis (10017888) (Gastroenteritis (10017888)) [v.22.0] [10017888]

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 HEMATEMESIS

- Investigator: Subject experienced gastroenteritis and hematemesis related to family members experiencing the same thing.

- AbbVie: Event is more likely a complication of gastroenteritis. Additional risk factor includes pre-existing history of peptic ulcer disease.

Event of GASTROENTERITIS

- Investigator: Stomach virus

- AbbVie: Event is common in the general population. Additional risk factor includes family members with similar symptoms.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] AST:** 52 U/L (normal 15 to 37)

[redacted] **20[redacted] BIOPSY:** Gastric: BENIGN GASTRIC MUCOSA WITH MILD MUCOSAL EROSION, NO SIGNIFICANT INFLAMMATION NOTED. NO HELICOBACTER APPRECIATED Esophagus: SQUAMOUS AND GLANDULAR MUCOSA WITH AREAS OF ACUTE AND CHRONIC INFLAMMATION AND ULCERATION AND NECROSIS, FUNGAL STAINS NEGATIVE.

[redacted] **20[redacted] BUN:** 26 mg/dL (normal 6 to 21)

[redacted] **20[redacted] CALCIUM:** 8.7 mg/dL (normal 9.1 to 10.3)

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** NO DEFINITE FINDING TO EXPLAIN ETIOLOGY OF HEMATEMESIS

[redacted] **20[redacted] EGD:** GRADE C ESOPHAGITIS , HIATAL HERNIA, NONOBSTRUCTIVE SCHATZKI'S RING AND GASTRITIS

[redacted] **20[redacted] GLUCOSE:** 157 mg/dL (normal 70 to 109)

[redacted] **20[redacted] HCT:** 29 % (normal 36 to 47)

[redacted] **20[redacted] HGB:** 9.5 G/DL (normal 12 to 16)

[redacted] **20[redacted] INVESTIGATION:** GASTRIC EMPTYING STUDY: No evidence of delayed gastric emptying

[redacted] **20[redacted] POTASSIUM:** 3.4 MMOL/L (normal 3.5 to 5.3)

[redacted] **20[redacted] RBC:** 3.07 X10**6/MCL (normal 3.8 to 5.4)

[redacted] **20[redacted] ULTRASOUND RUQ:** NORMAL RIGHT UPPER QUADRANT ULTRASOUND

[redacted] **20[redacted] URINE:** cloudy

[redacted] **20[redacted] VENOUS DOOPPLER OF UPPER EXTREMITY:** HROMBOSIS OF THE RIGHT PROXIMAL MID AND DISTAL CEPHALIC VEIN

[redacted] **20[redacted] X-RAY RIGHT KNEE:** DEGENERATIVE OSTEOARTHRITIS NEGATIVE FOR ACUTE INJURY

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
全身性エリテマトーデス	X	X		

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	8[redacted]	FEMALE	WHITE

Medical History	Onset Year
OBESITY	19[redacted]
HYPERTENSION	19
OTHER: POST MENOPAUSAL	19
OSTEOPOROSIS	20
OTHER: OVERACTIVE BLADDER	20
OTHER: FRACTURED PELVIS	20
OTHER: PLAQUE PSORIASIS	20
OTHER: SPINAL STENOSIS (LUMBAR REGION)	20
HYPOTHYROIDISM	20
OSTEOARTHRITIS: BOTH KNEES	20
DEPRESSION: MILD	20
OTHER: ANXIETY	20
OTHER: RESTLESS LEG SYNDROME	20

Prior Procedures	Procedure Year
SURGERY: TUBAL LIGATION	19[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 50	50

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
TOLTERODINE	4 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1.2 mg	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
COLECALCIFEROL	4000 IU	QD	Y-M: 20[redacted]
FUROSEMIDE	20 mg	PRN	Y-M: 20[redacted]
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]
FISH OIL	2000 mg	QD	Y-M: 20[redacted]
LEVOTHYROXINE	200 ug	QD	Y-M: 20[redacted]
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 20[redacted]
POTASSIUM	1 OTHER: TABLET	QD	Y-M: 20[redacted]
ALENDRONIC ACID	70 mg	EVERY WEEK	Y-M: 20[redacted]
GABAPENTIN	100 mg	PRN	Y-M: 20[redacted]
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
PAROXETINE	40 mg	QD	Y-M: 20[redacted] / -238

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
TOLTERODINE	4 mg	QD	Y-M: 20[redacted]	ONGOING
FOLIC ACID	1.2 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	4000 IU	QD	Y-M: 20[redacted]	ONGOING
FUROSEMIDE	20 mg	PRN	Y-M: 20[redacted]	ONGOING
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 67
FISH OIL	2000 mg	QD	Y-M: 20[redacted]	ONGOING
LEVOTHYROXINE	200 ug	QD	Y-M: 20[redacted]	ONGOING
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
POTASSIUM	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
ALENDRONIC ACID	70 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
GABAPENTIN	100 mg	PRN	Y-M: 20[redacted]	ONGOING
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]	ONGOING
PAROXETINE	40 mg	QD	Y-M: 20[redacted] / -238	ONGOING
CEFALEXIN	500 mg	BID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 59
ACICLOVIR	800 mg	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 60
TRAMADOL	50 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 61	ONGOING
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 68
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 68
VICODIN	325/5 mg	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 68
BISACODYL	10 mg	QD	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 69
DOCUSATE	100 mg	BID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 69
MAGNESIUM HYDROXIDE	30 mL	BID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 69
SIMETICONE	30 mL	PRN	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 69
TEMAZEPAM	15 mg	PRN	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 69
BUSPIRONE	5 mg	BID	Y-M: 20[redacted] / 62	ONGOING

ENOXAPARIN	40 mg	QD	Y-M: 20[redacted]-[redacted] / 62	ONGOING
IPRATROPIUM W/SALBUTAMOL	3 mL	QID	Y-M: 20[redacted]-[redacted] / 62	ONGOING
PARACETAMOL	650 mg	OTHER: EVERY 4 HOURS	Y-M: 20[redacted]-[redacted] / 62	Y-M: 20[redacted]-[redacted] / 68
LIDOCAINE	5 mL	QD	Y-M: 20[redacted]-[redacted] / 64	Y-M: 20[redacted]-[redacted] / 64
METOPROLOL	25 mg	BID	Y-M: 20[redacted]-[redacted] / 68	ONGOING
SALBUTAMOL	90 ug	PRN	Y-M: 20[redacted]-[redacted] / 70	ONGOING
PREDNISONE	40 mg	QD	Y-M: 20[redacted]-[redacted] / 71	ONGOING

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

Event Description	SYSTEMIC LUPUS ERYTHEMATOSUS
Preferred term	全身性エリテマトーデス
AE Onset Date / Rx Day	[redacted]20[redacted] / 42
Age at AE Onset	8[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 58): Erythrocyte Sedimentation Rate: 77 [NOT REPORTED - 30] mm/h; Leukocytes: 10.7 [3.8 - 10.8] 10^9/L; Monocytes: 1.124 [0.2 - 0.95] 10^9/L; NPTST030-C-REACTIVE PROTEIN: 206.2 [NOT REPORTED - 8] mg/L; Neutrophils: 8.314 [1.5 - 7.8] 10^9/L; [redacted]20[redacted] (RX DAY 62): NPTST009-ANA: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 67): NPTST127-SSA: NEAGTIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST128-SSB AB: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUBJECTS WITH AUTOIMMUNE DISORDERS SUCH AS PLAQUE PSORIASIS, PSORIATIC ARTHRITIS, AND HYPOTHYROIDISM MAY BE MORE LIKELY TO DEVELOP SYSTEMIC LUPUS ERYTHEMATOSUS.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 8[redacted] 歳女性であり，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，全身性エリテマトーデスの事象を発現した。

Event 1 の臨床経過：

関連する病歴は元タバコ使用者（25 年間，1 日 1 箱）及び乾癬性関節炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は全身性エリテマトーデスを発現した。

入院前，被験者は 3 週間にわたって発熱を来した。担当医は帯状疱疹の可能性を除外し，感染症とリウマチ疾患の検査のために入院することを勧めた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は，息切れ，鈍い痛み，鋭い痛み，倦怠感，疲労及び発熱を呈していた。WBC スキャン検査により感染症は認められず，気管支鏡検査の仮結果も感染症なしであった。ANA は陽性であった。腰痛，右股関節痛及び右膝関節痛を発現した。また，頭皮乾癬も認められた。それ以外は，全身所見に異常は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，トラマドール，ケフレックス，アセトアミノフェン・ヒドロコドン合剤，アセトアミノフェン，acyclovir 及び prednisone であった。

Causality for ABT-494 (Blinded)

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1) Systemic lupus erythematosus (10042945) (Systemic lupus erythematosus (10042945)) [v.21.0] [10042945]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of SYSTEMIC LUPUS ERYTHEMATOSUS

- Investigator: SUBJECTS WITH AUTOIMMUNE DISORDERS SUCH AS PLAQUE PSORIASIS, PSORIATIC ARTHRITIS, AND HYPOTHYROIDISM MAY BE MORE LIKELY TO DEVELOP SYSTEMIC LUPUS ERYTHEMATOSUS.

- AbbVie: SUBJECTS WITH AUTOIMMUNE DISORDERS SUCH AS PLAQUE PSORIASIS, PSORIATIC ARTHRITIS, AND HYPOTHYROIDISM MAY BE MORE LIKELY TO DEVELOP SYSTEMIC LUPUS ERYTHEMATOSUS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANA:** 1:640 (ratio), Positive

Unknown date ANTIBODY TEST: SSA, SSB antibody tests negative

[redacted] **20[redacted] BRONCHOSCOPY:** Preliminarily negative for infection.

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 206.2 MG/L (normal <8)

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 77 MM/HR (normal <30)

[redacted] **20[redacted] INDIUM LABELED WBC SCAN:** Negative for infection.

[redacted] **20[redacted] MONOCYTES ABS:** 1124 cells/uL (normal 200 to 950)

[redacted] **20[redacted] NEUTROPHILS ABS:** 8314 cells/uL (normal 1500 to 7800)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 10.7 X10**3/MCL (normal 3.8 to 10.8)

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
胆石症	X			
処置後胆汁漏出	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 15 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: APPENDICITIS	19[redacted]
TUBERCULOSIS: LATENT TUBERCULOSIS	19
DEPRESSION: RECURRENT, MILD	19
OTHER: EXCESSIVE VAGINAL BLEEDING	19
OBESITY	20
ANEMIA: MILD	20
OSTEOARTHRITIS	20
OTHER: RIGHT MENISCAL TEAR	20
OTHER: RADICULOPATHY (LUMBAR REGION)	20
OTHER: SPONDYLOSIS WITHOUT MYELOPATHY	20
GASTROESOPHAGEAL REFLUX DISEASE	20
HYPERTENSION	20
HYPOTHYROIDISM	20
OTHER: PLAQUE PSORIASIS	20
DRUG ALLERGIES/REACTIONS: PLAQUENIL ALLERGY	20
OTHER: ASTHMATIC BRONCHITIS	20
OTHER: VITAMIN D DEFICIENCY	20
OTHER: CARPAL TUNNEL SYNDROME (RIGHT UPPER LIMB)	20
OTHER: OCCASIONAL DIARRHEA	20

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	19[redacted]
SURGERY: HYSTERECTOMY	19[redacted]
SURGERY: TOTAL KNEE ARTHROPLASTY (RIGHT)	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ISONIAZID	5 mg/kg	QD	Y-M: 19[redacted]
HYDROCHLOROTHIAZIDE W/LOSARTAN	100/12.5 mg	QD	Y-M: 20[redacted]
LEVOTHYROXINE	100 ug	QD	Y-M: 20[redacted]
LORAZEPAM	0.5 mg	PRN	Y-M: 20[redacted]
METHOCARBAMOL	500 mg	PRN	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
DICLOFENAC	1 OTHER: APPLICATION	QID	Y-M: 20[redacted]
PIROXICAM	20 mg	QD	Y-M: 20[redacted]
HYDROXYCHLOROQUINE	400 mg	QD	Y-M: 20[redacted]
DICLOFENAC	170 mg	PRN	Y-M: 20[redacted]
ERGOCALCIFEROL	1000 IU	BID	Y-M: 20[redacted]
FOLIC ACID	3 mg	QD	Y-M: 20[redacted]
METHOTREXATE	0.8 mL	EVERY WEEK	Y-M: 20[redacted]
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 20[redacted]
SULFASALAZINE	500 mg	QD	Y-M: 20[redacted]
TRAMADOL	50 mg	QID	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
GLUCOSAMINE & CHONDROITIN WITH MSM	400/500/250 mg	QD	Y-M: 20[redacted]
LOPERAMIDE	1 OTHER: TABLET	PRN	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: ONCE PER MONTH	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
HYDROCHLOROTHIAZIDE W/LOSARTAN	100/12.5 mg	QD	Y-M: 20[redacted]	Not reported.
LEVOTHYROXINE	100 ug	QD	Y-M: 20[redacted]	Not reported.
LORAZEPAM	0.5 mg	PRN	Y-M: 20[redacted]	Not reported.
METHOCARBAMOL	500 mg	PRN	Y-M: 20[redacted]	Not reported.
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 463
DICLOFENAC	1 OTHER: APPLICATION	QID	Y-M: 20[redacted]	Not reported.
PIROXICAM	20 mg	QD	Y-M: 20[redacted]	Not reported.
DICLOFENAC	170 mg	PRN	Y-M: 20[redacted]	Not reported.
ERGOCALCIFEROL	1000 IU	BID	Y-M: 20[redacted]	Not reported.
FOLIC ACID	3 mg	QD	Y-M: 20[redacted]	Not reported.
METHOTREXATE	0.8 mL	EVERY WEEK	Y-M: 20[redacted]	Not reported.
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]	Not reported.
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Not reported.
TRAMADOL	50 mg	QID	Y-M: 20[redacted]	Not reported.
GLUCOSAMINE & CHONDROITIN WITH MSM	400/500/250 mg	QD	Y-M: 20[redacted]	Not reported.
LOPERAMIDE	1 OTHER: TABLET	PRN	Y-M: 20[redacted]	Not reported.
SALBUTAMOL	90 ug	PRN	Y-M: 20[redacted] / 214	Not reported.
RANITIDINE	75 mg	QD	Y-M: 20[redacted] / 464	Not reported.
ACICLOVIR	800 mg	OTHER: 5 TIMES PER DAY	Y-M: 20[redacted] / 471	Y-M: 20[redacted] / 478
ONDANSETRON	4 mg	QD	Y-M: 20[redacted] / 475	Y-M: 20[redacted] / 475
HYDROMORPHONE	0.5 mg	QD	Y-M: 20[redacted] / 475	Y-M: 20[redacted] / 477
MORPHINE	2 mg	QD	Y-M: 20[redacted] / 475	Y-M: 20[redacted] / 477
SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 475	Y-M: 20[redacted] / 477
DOCUSATE	100 mg	QD	Y-M: 20[redacted] / 475	Y-M: 20[redacted] / 478
OXYCOCET	5/325 mg	QD	Y-M: 20[redacted] / 475	Y-M: 20[redacted] / 488
CEFOTETAN	2 g	QD	Y-M: 20[redacted] / 476	Y-M: 20[redacted] / 476
FLEBOBAG RING LACT	1000 mL	QD	Y-M: 20[redacted] / 476	Y-M: 20[redacted] / 476

INDOMETACIN	100 mg	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 476 / 476
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 476 / 477
HEPARIN	1 mL	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 476 / 478

Event #1: Serious Adverse Event

Event Description	CHOLELITHIASIS
Preferred term	胆石症
AE Onset Date / Rx Day	[redacted]20[redacted] / 462
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 465): CHOLECYSTECTOMY: GALLBLADDER REMOVED. NO COMPLICATIONS.

AE Stopped Rx Day	466
Duration of AE	5 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	OBESITY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	BILIARY DUCT LEAK (PROCEDURAL INJURY)
Preferred term	処置後胆汁漏出
AE Onset Date / Rx Day	[redacted]20[redacted] / 475
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 476): BILIARY SPHINCTEROTOMY WITH PLASTIC STENT PLACEMENT: COMPLETED WITH NO COMPLICATIONS; [redacted]20[redacted] (RX DAY 477): CT SCAN ABDOMEN/PELVIS: 3.7 CM SUB HEPATIC FLUID COLLECTION

AE Stopped Rx Day	476
Duration of AE	2 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CHOLECYSTECTOMY
Discontinued Study Drug Due to the	NO

Event
SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，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，胆石症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は虫垂切除，虫垂炎，肥満，胃食道逆流性疾患，高血圧，局面型乾癬，乾癬性関節炎，元喫煙者（1 日 0.3 箱を 3 年間）及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胆石症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胆石症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腹痛のため救急治療室を受診したが，帰宅させられた。20[redacted] 年 [redacted] 月 [redacted] 日，同病院を再受診し，胆石症のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，胆嚢切除術が行われた。合併症は生じなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は予約していた担当外科医による経過観察を受けた。問題や合併症は認められなかった。

The patient's past medications include:

ISONIAZID for LATENT TUBERCULOSIS (19[redacted] - 19[redacted])

PLAQUENIL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SULFASALAZINE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

COSENTYX for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Cholelithiasis (10008629) (Cholelithiasis (10008629)) [v.22.0] [10008629]

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 CHOLELITHIASIS

- Investigator: Obesity.

- AbbVie: Risk factors include age, gender and obesity.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CHEST X-RAY: Normal
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，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，両側胆管漏出（処置に伴う損傷）の事象を発現した。

Event 2 の臨床経過：

関連する病歴は元喫煙者（1 日 0.3 箱を 3 年間），肥満，高血圧，局面型乾癬，乾癬性関節炎及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両側胆管漏出（処置に伴う損傷）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，両側胆管漏出（処置に伴う損傷）は消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胆石症の重篤な事象を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胆嚢切除術が行われ，問題や合併症は生じなかった（AER No.19P-163-2894723-00）。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は亜急性の右腹部痛のため救急治療室を受診し，先日の胆嚢切除術による両側胆管漏出と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，総胆管括約筋切開術とプラスチックステント留置が行われた。合併症は生じなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，オキシコドン及びアセトアミノフェンであった。

The patient's past medications include:

ISONIAZID for LATENT TUBERCULOSIS (19[redacted] - 19[redacted])

PLAQUENIL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SULFASALAZINE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

COSENTYX for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Post procedural bile leak (10057586) (Post procedural bile leak (10057586)) [v.22.0] [10057586]

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 BILIARY DUCT LEAK (PROCEDURAL INJURY)

- Investigator: Cholecystectomy.

- AbbVie: Event is more likely a complication of recent cholecystectomy procedure.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT SCAN ABDOMEN/PELVIS:** 3.7 cm sub hepatic fluid collection.

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
不安定狭心症	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
OBESITY: MORBID	19[redacted]
ASTHMA	20
HYPERTENSION	20
OTHER: ATHEROSCLEROSIS OF AORTA	20
OTHER: HYPERTENSIVE HEART DISEASE (WITHOUT HEART FAILURE)	20
OTHER: SLEEP APNEA	20
DIABETES MELLITUS: TYPE II	20
OTHER: SOLITARY PULMONARY NODULE (BENIGN)	20
OTHER: CERVICAL AND LUMBAR RADICULOPATHY	20
OTHER: CHRONIC LOW BACK PAIN	20
HYPERLIPIDEMIA: MILD	20
OTHER: CARPAL TUNNEL SYNDROME	20
GASTROESOPHAGEAL REFLUX DISEASE	20
PERIPHERAL NERVE DISORDER: DIABETIC PERIPHERAL NEROPATHY	20
DEPRESSION: MILD, CONTROLLED	20
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20
OTHER: ANXIETY	20
OTHER: PLAQUE PSORIASIS	20
OTHER: SEASONAL ALLERGIES	20
OTHER: MORPHINE DRUG ALLERGY	20
OTHER: ELEVATED TRIGLYCERIDES	20
OTHER: PULMONARY FIBROSIS	20
TUBERCULOSIS: LATENT	20

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 167	167
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 168	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FUROSEMIDE	20 mg	QD	Y-M: 20[redacted]
GLIPIZIDE	5 mg	QD	Y-M: 20[redacted]
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]
SPIRONOLACTONE	25 mg	QD	Y-M: 20[redacted]
SIMVASTATIN	10 mg	QD	Y-M: 20[redacted]
RANITIDINE	300 mg	QD	Y-M: 20[redacted]
METOPROLOL	25 mg	QD	Y-M: 20[redacted]
SALBUTAMOL	2.5 mg	PRN	Y-M: 20[redacted]
DULOXETINE	60 mg	QD	Y-M: 20[redacted]
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]
BUDESONIDE W/FORMOTEROL FUMARATE	320/9 ug	BID	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
DICLOFENAC	100 mg	QD	Y-M: 20[redacted]
BUPROPION	150 mg	QD	Y-M: 20[redacted]
COLECALCIFEROL	50000 IU	EVERY WEEK	Y-M: 20[redacted]
FISH OIL	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
GABAPENTIN	600 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]-[redacted] / -329
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]-[redacted] / -329
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted] / -329
CLOBETASOL	1 OTHER:	BID	Y-M: 20[redacted]-[redacted] / -47

	APPLICATION		
HYDROCORTISONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -47
TRIAMCINOLONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -47
NICOTINE	14 mg	QD	Y-M: 20[redacted] / -23
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -19
PYRIDOXINE	50 mg	QD	Y-M: 20[redacted] / -19

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FUROSEMIDE	20 mg	QD	Y-M: 20[redacted]	Not reported.
GLIPIZIDE	5 mg	QD	Y-M: 20[redacted]	Not reported.
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]	Not reported.
SPIRONOLACTONE	25 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 30
SIMVASTATIN	10 mg	QD	Y-M: 20[redacted]	Not reported.
RANITIDINE	300 mg	QD	Y-M: 20[redacted]	Not reported.
METOPROLOL	25 mg	QD	Y-M: 20[redacted]	Not reported.
SALBUTAMOL	2.5 mg	PRN	Y-M: 20[redacted]	Not reported.
DULOXETINE	60 mg	QD	Y-M: 20[redacted]	Not reported.
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]	Not reported.
BUDESONIDE W/FORMOTEROL FUMARATE	320/9 ug	BID	Y-M: 20[redacted]	Not reported.
DICLOFENAC	100 mg	QD	Y-M: 20[redacted]	Not reported.
BUPROPION	150 mg	QD	Y-M: 20[redacted]	Not reported.
COLECALCIFEROL	50000 IU	EVERY WEEK	Y-M: 20[redacted]	Not reported.
FISH OIL	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]	Not reported.
GABAPENTIN	600 mg	QD	Y-M: 20[redacted]	Not reported.
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -19	Not reported.
PYRIDOXINE	50 mg	QD	Y-M: 20[redacted] / -19	Not reported.
ACETYLSALICYLIC ACID	325 mg	QD	Y-M: 20[redacted] / 28	Not reported.
GLYCERYL TRINITRATE	0.4 mg	QD	Y-M: 20[redacted] / 28	Not reported.
GLUCOSE	50 %	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
GLYCERYL TRINITRATE	0.4 mg	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
MAGNESIUM	100 mL	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] /

NABUMETONE	750 mg	BID	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-29
PARACETAMOL	325 mg	PRN	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-29
COMBIVENT	3 mL	PRN	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
FLEBOBAG RING LACT	1000 mL	QD	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
GLUCAGON	1 mg	PRN	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
GLUCOSE	4 g	QD	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
GLUCOSE	50 mL	PRN	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
INSULIN LISPRO	100 OTHER: U/ML	QD	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
MAGNESIUM	50 mL	QD	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
POTASSIUM	1 OTHER: DOSE	QD	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
POTASSIUM	20 mEq	QD	Y-M: 20[redacted]-28 / Y-M: 20[redacted]-30
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]-29 / Y-M: 20[redacted]-30
SODIUM CHLORIDE	2000 mL	QD	Y-M: 20[redacted]-29 / Y-M: 20[redacted]-30
DIPHENHYDRAMINE	50 mg	QD	Y-M: 20[redacted]-30 / Y-M: 20[redacted]-30
FENTANYL	100 ug	QD	Y-M: 20[redacted]-30 / Y-M: 20[redacted]-30
GLYCERYL TRINITRATE	100 ug	QD	Y-M: 20[redacted]-30 / Y-M: 20[redacted]-30
HEPARIN	5000 OTHER: UNITS	QD	Y-M: 20[redacted]-30 / Y-M: 20[redacted]-30
LIDOCAINE		QD	Y-M: 20[redacted]-30 / Y-M: 20[redacted]-30
LIDOCAINE	50 mL	QD	Y-M: 20[redacted]-30 / Y-M: 20[redacted]-30
VERAPAMIL	2.5 mg	QD	Y-M: 20[redacted]-30 / Y-M: 20[redacted]-30

Event #1: Serious Adverse Event

Event Description	UNSTABLE ANGINA PECTORIS

Preferred term	不安定狭心症
AE Onset Date / Rx Day	[redacted]20[redacted] / 28
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 30): Blood Urea Nitrogen: 7.5 [2.5 - 6.43] mmol/L; Creatinine: 73.37 [48.62 - 106.08] umol/L; Glucose: 6.83 [4.11 - 5.88] mmol/L; Hemoglobin: 121 [114 - 151] g/L; Leukocytes: 12 [4.2 - 11.1] 10^9/L; Platelets: 205 [130 - 400] 10^9/L; Sodium: 135 [136 - 145] mmol/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 28): CHEST X RAY: ACUTE BRONCHITIS VERSUS INTERSTITIAL PULMONARY EDEMA; [redacted]20[redacted] (RX DAY 29): VL EXTREMITY ART LOVER BILAT: NO EVIDENCE OF SIGNIFICANT STENOSIS; VL SEG/PRESSURE SINGLE: NO EVIDENCE OF SIGNIFICANT STENOSIS; [redacted]20[redacted] (RX DAY 30): LEFT HEART CATHETERIZATION: NORMAL

AE Stopped Rx Day	32
Duration of AE	5 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FAMILY HISTORY OF CARDIAC EVENTS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳女性であり，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，不安定狭心症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は病的肥満，喘息，アテローム性大動脈硬化症，高血圧，高血圧性心疾患（心不全なし），睡眠時無呼吸，2 型糖尿病，孤立性肺結節，高脂血症，胃食道逆流性疾患，不安，コントロール下の軽度のうつ病，肺気腫／慢性閉塞性肺疾患，局面型乾癬，乾癬性関節炎，トリグリセリド増加，肺線維症，喫煙者（1 日 0.25 箱を 14 年間）及び現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は不安定狭心症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，不安定狭心症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日の夕方，被験者は胸痛が 3 日間続いたため救急科を受診した。胸痛は横になっていても消失しなかった。被験者によると，胸痛は胸骨下の胸部の圧迫感及び絞扼感で，診察時にも認められた。胸痛は，呼吸困難，動悸及び浮動性めまいを伴っていた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はその後，心臓の検査のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，左心カテーテル検査が行われた。結果は正常であった。

病院の記録：

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸痛が 3 日間続いたため救急科を受診した。胸痛は横になっていても消失しなかった。胸痛は胸骨下の胸部の圧迫感及び絞扼感で，絞扼感は胸骨下で発現し，上部に放散して，口腔内に金属味／酸味を感じた。胸痛は診察時にも認められ，間欠性で，最もひどい時で 10 点中 6 点であった。被験者によると，何をしても軽減したり増悪したりすることはなかった。胸痛は，呼吸困難，動悸及び浮動性めまいを伴っていた。被験者は下肢動脈狭窄及び心肥大を呈していると述べた。その他の体質的な症状はなかった。トロポニンを 2 回測定したが，いずれも異常なしであったため，急性冠動脈症候群の可能性は除外された。20[redacted] 年 [redacted] 月 [redacted] 日，胸部 X 線検査により肺水腫ではなく急性気管支炎が認められた。WBC が 12.7 に増加した。20[redacted] 年 [redacted] 月 [redacted] 日，左心カテーテル検査の結果は正常で，CAD は認められず，LVEF も 60%と正常であった。下肢動脈の検査が行われたが，結果はやはり正常で，著しい狭窄も認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，nitrostat，アセトアミノフェン，pepcid，ナブメトン，ニトログリセリン，アスピリン及び calan であった。

The patient's past medications include:

CLOBETASOL 0.05% for PSORIASIS (20[redacted] - 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

FOLIC ACID for SUPPLEMENT TO MTX USE ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HYDROCORTISONE for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TRIAMCINOLONE ACETONIDE for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Angina pectoris unstable (10002385) (Angina unstable (10002388)) [v.22.0] [10002385]

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 UNSTABLE ANGINA PECTORIS

- Investigator: FAMILY HISTORY OF CARDIAC EVENTS

- AbbVie: More likely related to underlying risk factors of hypertension, diabetes, obesity, hypertensive heart disease, hyperlipidemia, aortic atherosclerosis and smoking.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE:** 150/91mmHg

[redacted] **20[redacted] BMI:** 61.9 kg/m2

[redacted] **20[redacted] BUN:** 21 mg/dL (normal 7 to 18)

[redacted] **20[redacted] CHEST X-RAY:** Abnormal Finding. Calcified granulomas : Present, No pleural thickening, No Pleural Scarring, No Signs of Active TB. Finding indicative of previous TB infection. Other Findings: Granuloma, Cardiomegaly, Mild pulmonary inflation.

[redacted] **20[redacted] CHEST X-RAY:** ACUTE BRONCHITIS VERSUS INTERSTITIAL PULMONARY EDEMA

[redacted] **20[redacted] CREATININE:** Results: 0.83 mg/dL Lower normal range: >0.55 Upper normal range: <1.2

[redacted] **20[redacted] ECG:** Abnormal; Low QRS voltage in chest leads.

[redacted] **20[redacted] ECG:** Results not provided

[redacted] **20[redacted] BLOOD GLUCOSE:** Results: 123 mg/dL Lower normal range: >74 Upper normal range: <106

[redacted] **20[redacted] HCT:** 36.6 % (normal 36.1 to 45.4)

[redacted] **20[redacted] HEMOGLOBIN:** Results: 12.1 g/dL Lower normal range: >11.4 Upper normal range: < 15.1

[redacted] **20[redacted] HGB:** 12.1 G/DL (normal 11.4 to 15.1)

[redacted] **20[redacted] LEFT HEART CATHETERIZATION:** Normal coronary artery with normal left ventricular systolic function

[redacted] **20[redacted] PLATELET COUNT:** Results: 205 K/UL Lower normal range: >130 Upper normal range: < 400

[redacted] **20[redacted] PLT:** 205 K/uL (normal 130 to 400)

[redacted] **20[redacted] POTASSIUM:** 4 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] PULSE:** 65 /min

[redacted] **20[redacted] RESPIRATORY RATE:** 14 /min

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

[redacted] **20[redacted] TEMP:** 98.2 F

[redacted] **20[redacted] TROPONIN:** Done twice. Negative both times.

[redacted] **20[redacted] VL EXTREMITY ART LOVER BILATERAL:** NO EVIDENCE OF SIGNIFICANT STENOSIS

[redacted] **20[redacted] VL SEG/PRESSURE SINGLE:** NO EVIDENCE OF SIGNIFICANT STENOSIS

[redacted] **20[redacted] WBC:** 12.7 No units

[redacted] **20[redacted] WBC:** 12.0 K/ul

[redacted] **20[redacted] WEIGHT:** 142.9 KG

[redacted] **20[redacted] WHITE BLOOD CELLS:** Results: 12 K/UL Lower normal range: >4.2 Upper normal range: < 11.1

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
急性呼吸不全	X	X		X
失血性貧血	X	X		X
心肺停止	X	X		X
びらん性胃炎	X	X		
肺炎	X	X		X
肺塞栓症	X	X		X
心室細動	X	X		

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	7[redacted]	FEMALE	WHITE

Medical History	Onset Year
OBESITY	19[redacted]
DRUG ALLERGIES/REACTIONS: ADHESIVE BANDAGE	19[redacted]
DRUG ALLERGIES/REACTIONS: LATEX	19[redacted]
OTHER: UTERINE FIBROIDS	19[redacted]
DRUG ALLERGIES/REACTIONS: BERRY DECONGESTANT	19[redacted]
DRUG ALLERGIES/REACTIONS: MEFOXIN	19[redacted]
HYPERTENSION	19[redacted]
OTHER: BILATERAL LEG EDEMA	19[redacted]
OTHER: POTASSIUM DEFICIENCY	19[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO CELEBREX	19[redacted]
OTHER: LOW BACK PAIN	19[redacted]
OSTEOARTHRITIS: BILATERAL HANDS	20[redacted]
OSTEOARTHRITIS: BILATERAL KNEES	20[redacted]
DRUG ALLERGIES/REACTIONS: GLUTENS	20[redacted]
DRUG ALLERGIES/REACTIONS: WHEAT	20[redacted]
DRUG ALLERGIES/REACTIONS: LYRICA	20[redacted]
HYPERLIPIDEMIA: DIET CONTROLLED	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: ANEMIA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY	19[redacted]
SURGERY: BACK SURGERY SECONDARY TO MOTOR VEHICLE ACCIDENT	19[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / [redacted] 1	[redacted]F[redacted]20[redacted] / [redacted] 160	160

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LISINOPRIL	5 mg	QD	Y-M: 19[redacted]
FUROSEMIDE	40 mg	QD	Y-M: 19[redacted]
POTASSIUM	10 mEq	QD	Y-M: 19[redacted]
METHOTREXATE	20 mg	QD	Y-M: 20[redacted]
NAPROXEN	750 mg	PRN	Y-M: 20[redacted]
SULFASALAZINE	2500 mg	QD	Y-M: 20[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
PANADEINE CO	30/300 mg	PRN	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted] / -287
BIOTIN	10 mg	QD	Y-M: 20[redacted] / -262
FISH OIL	630 mg	QD	Y-M: 20[redacted] / -262
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted] / -89

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LISINOPRIL	5 mg	QD	Y-M: 19[redacted]	ONGOING
FUROSEMIDE	40 mg	QD	Y-M: 19[redacted]	ONGOING
POTASSIUM	10 mEq	QD	Y-M: 19[redacted]	ONGOING
PANADEINE CO	30/300 mg	PRN	Y-M: 20[redacted]	ONGOING
BIOTIN	10 mg	QD	Y-M: 20[redacted] / -262	ONGOING
FISH OIL	630 mg	QD	Y-M: 20[redacted] / -262	ONGOING
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted] / -89	ONGOING
PHENFLU G	1 OTHER: TABLESPOON	PRN	Y-M: 20[redacted] / 139	Y-M: 20[redacted] / 144
CISATRACURIUM	UNKNOWN OTHER: UNKNOWN	OTHER: ONCE	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 161
EPINEPHRINE	1 OTHER: DOSE	OTHER: ONCE	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 161
POTASSIUM	100 mL	OTHER: ONCE	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 163
HEPARIN	0.5 mL	OTHER: PRN	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 174

HYDROMORPHONE	1 mL	PRN	Y-M: 20[redacted] / Y-M: 20[redacted] / 161 175
INSULIN	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / Y-M: 20[redacted] / 161 175
OXYGEN	UNKNOWN OTHER: LITERS	OTHER: CONTINUOUS	Y-M: 20[redacted] / Y-M: 20[redacted] / 161 175
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 161 175
PIP/TAZO	12.5 mL	OTHER: EVERY 8 HOUR	Y-M: 20[redacted] / Y-M: 20[redacted] / 161 175
SODIUM CHLORIDE	250 mL	OTHER: CONTINOUS	Y-M: 20[redacted] / Y-M: 20[redacted] / 161 175
PROPOFOL	100 mL	OTHER: ONCE	Y-M: 20[redacted] / Y-M: 20[redacted] / 161 193
SODIUM CHLORIDE	UNKNOWN OTHER: UNKNOWN	OTHER: CONTINOUS	Y-M: 20[redacted] / Y-M: 20[redacted] / 163 163
APIXABAN	10 mg	BID	Y-M: 20[redacted] / Y-M: 20[redacted] / 175 181

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Study Specific Adverse Events of Interest, Positively Adjudicated Events

Event Description	ACUTE HYPOXIC RESPIRATORY FAILURE
Preferred term	急性呼吸不全
AE Onset Date / Rx Day	[redacted]20[redacted] / 161 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 161): HYPOTHERMIA PROTOCOL: REWARMED [redacted]20[redacted]; OROTRACHEALLY INTUBATED ON MECHANICAL VENTILATION: UNRESPONSIVE AT TIME, EXTUBATED 02MAR2018

AE Stopped Rx Day	175 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

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

Event Description	ACUTE BLOOD LOSS ANEMIA

Preferred term	失血性貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 161 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 161): Hemoglobin: 125 [120 - 160] g/L; Leukocytes: 6.4 [4.5 - 11] 10^9/L; [redacted]20[redacted] (RX DAY 162): Hemoglobin: 119 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 163): Hemoglobin: 102 [120 - 160] g/L; [redacted]20[redacted] (RX DAY 175): Hemoglobin: 89 [120 - 160] g/L

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NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 161): TRANSFUSION 1 UNIT OF BLOOD: HEMOGLOBIN STABILIZED; [redacted]20[redacted] (RX DAY 170): COLONOSCOPY: HEMORRHOIDS, DIVERTICULOSIS, ULCERS IN DISTAL RECTUM, NO BLEEDING; [redacted]20[redacted] (RX DAY 174): CAPSULE ENDOSCOPY: NORMAL SMALL BOWEL; UPPER GI ENDOSCOPY: MODERATE SEVERE ESOPHAGITIS, WITH NO BLEEDING

AE Stopped Rx Day	175 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Study Specific Adverse Events of Interest, Positively Adjudicated Events

Event Description	CARDIOPULMONARY ARREST
Preferred term	心肺停止
AE Onset Date / Rx Day	[redacted]20[redacted] / 161 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 161): NPTST028-BNP: 50.2 [NOT REPORTED - NOT REPORTED] ng/L; NPTST134-TROPONIN: 2.36 [NOT REPORTED - NOT REPORTED] ng/mL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 161): EKG: SINUS RHYTHM WITH CHANGES SUGGESTIVE OF LEFT VENTRICULAR HYPERTROPHY WITH QRS WIDENING, T WAVE ABNORMALITY, CONSIDER ANTERIOR ISCHEMIA

AE Stopped Rx Day	175 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

Event #4: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	EROSIVE GASTRITIS
Preferred term	びらん性胃炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 161 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 164): UPPER GI ENDOSCOPY: NON-REFLUX ESOPHAGITIS - NON-BLEEDING EROSIVE GASTROPATHY; [redacted]20[redacted] (RX DAY 170): COLONOSCOPY: MULTIPLE ULCERS IN DISTAL RECTUM, BIOPSIED, NO BLEEDING; [redacted]20[redacted] (RX DAY 174): CAPSULE ENDOSCOPY: NORMAL SMALL BOWEL (SMALL BOWEL PASSAGE 4 HOURS AND 20 MINUTES); UPPER GI ENDOSCOPY: ESOPHAGITIS, NO BLEEDING

AE Stopped Rx Day	175 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the	YES

Event	
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #8: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Study Specific Adverse Events of Interest

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 161 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 161): ANGIO CHEST WITH/WITHOUT CONTRAST CT SCAN: PULMONARY ARTERIAL EMBOLI, SECONDARY TO PE OR PNEUMONITIS, FLUID LEVEL WITH THE RIGHT LOWER LOBE BRONCHUS

AE Stopped Rx Day	175 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

Event #9: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Study Specific Adverse Events of Interest, Positively Adjudicated Events

Event Description	BILATERAL PULMONARY EMBOLI
Preferred term	肺塞栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 161 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
NOT REPORTED

AE Stopped Rx Day	175 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED

Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

Event #11: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	VENTRICULAR FIBRILLATION
Preferred term	心室細動
AE Onset Date / Rx Day	[redacted]20[redacted] / 161 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 161): CARDIOPULMONARY RESUSCITATION: UNRESPONSIVE; INTUBATED: EXTUBATED [redacted]20[redacted]; SHOCK DELIVERED 1 TIME: UNRESPONSIVE

AE Stopped Rx Day	161 (1 DAY AFTER LAST TREATMENT)
Duration of AE	1 DAY
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳女性であり，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，肺炎の疑い，心肺停止，両側肺塞栓症，急性低酸素血症性呼吸不全，急性失血性貧血，びらん性胃炎及び心室細動の事象を発現した。

Event 1～4、8、9 及び 11 の臨床経過：

関連する病歴は肥満，高血圧，両脚浮腫，自動車事故後の背部手術，局面型乾癬，乾癬性関節炎，非喫煙者，非飲酒者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎の疑い，心肺停止，両側肺塞栓症，急性低酸素血症性呼吸不全，急性失血性貧血，びらん性胃炎及び心室細動を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，心室細動は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎の疑い，心肺停止，両側肺塞栓症，急性低酸素血症性呼吸不全，急性失血性貧血及びびらん性胃炎は消失した。

治験薬の投与は 20[redacted] 年 [redacted] 月 [redacted] 日に完全に中止された。被験者の夫は，被験者が歩行器を使用してトイレに向かって歩いているときによだれを垂らしていることに気づいた。被験者は失神し，息切れをしていた。被験者は呼吸が困難な状態で，夫が被験者をゆっくり床に座らせたが，そのとき夫は被験者が呼吸しようとあえいでいることに気づいた。EMS 到着時，被験者は無反応で呼吸をしていなかったが，まだ脈はあった。CPR 及び挿管が行われた。その後，脈拍が消失し，被験者は心室細動に陥った。CPR と除細動が 1 回行われた。被験者が救急治療室に到着した際，被験者は完全に無反応であり，不自然な姿勢で完全にぐったりしていた。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に集中治療室に入院した。集中治療室で被験者は挿管されたまま依然として無反応であった。被験者は高血糖及び低カリウム血症を呈しており，テレメトリーで心不整脈が検出された。低体温療法プロトコルに従った手順が行われ，胸部 CAT により両側肺塞栓症が認められた。被験者は肺炎を発症し，抗生物質が投与された。また，褐色嘔吐を伴ってヘモグロビンが減少し，EGD などの消化管検査でびらん性胃炎が認められた。その後，結腸内視鏡検査により直腸潰瘍が認められたが，肥厚や出血は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，血液 1 単位が輸血され，ヘモグロビン値は安定した。20[redacted] 年 [redacted] 月 [redacted] 日，抜管が行われた。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に退院し，息切れや胸痛の訴えはなかった。

投与された薬剤は，ゾシン，ドキシサイクリン，アルブテロール・イプラトロピウム合剤，ヒドロモルフォン，レベチラセタム，インスリン，pantoprazole，プロポフォール，酸素，エリキュース，ヘパリン GTT，epinephrine 及び塩化カリウムであった。

The patient's past medications include:

CELEBREX for UNKNOWN INDICATION

LYRICA for UNKNOWN INDICATION

MEFOXIN for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.21.0] [10035664]

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

2) Cardiopulmonary arrest (10007644) (Cardio-respiratory arrest (10007617)) [v.21.0] [10007644]

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) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.21.0] [10037377]

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

4) Acute respiratory failure (10001053) (Acute respiratory failure (10001053)) [v.21.0] [10001053]

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

5) Acute post hemorrhagic anemia (10057221) (Haemorrhagic anaemia (10052293)) [v.21.0] [10057221]

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

6) Gastritis erosive (10017865) (Gastritis erosive (10017865)) [v.21.0] [10017865]

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

7) Ventricular fibrillation (10047290) (Ventricular fibrillation (10047290)) [v.21.0] [10047290]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of PROBABLE PNEUMONIA

- Investigator: NOT APPLICABLE

- AbbVie: EVENT IS MORE LIKELY RELATED TO BILATERAL PULMONARY EMBOLISM.

Event of CARDIOPULMONARY ARREST

- Investigator: NOT APPLICABLE

- AbbVie: EVENT IS MORE LIKELY RELATED TO BILATERAL PULMONARY EMBOLI.

Event of BILATERAL PULMONARY EMBOLI

- Investigator: NOT APPLICABLE

- AbbVie: RISK FACTORS INCLUDE PRE-EXISTING OBESITY AND PSORIATIC ARTHRITIS WITH CURRENT DMARD USE. (OGDIE A. RISK OF VENOUS THROMBOEMBOLISM IN PATIENTS WITH PSORIATIC ARTHRITIS, PSORIASIS AND RHEUMATOID ARTHRITIS: A GENERAL POPULATION-BASED COHORT STUDY. EUROPEAN HEART JOURNAL. 2017; APRIL 20.)

Event of ACUTE HYPOXIC RESPIRATORY FAILURE

- Investigator: NOT APPLICABLE

- AbbVie: EVENT IS MORE LIKELY RELATED TO PNEUMONIA AND BILATERAL PULMONARY EMBOLI.

Event of ACUTE BLOOD LOSS ANEMIA

- Investigator: NOT APPLICABLE

- AbbVie: EVENT IS MORE LIKELY RELATED TO EROSIVE GASTRITIS.

Event of EROSIVE GASTRITIS

- Investigator: NOT APPLICABLE

- AbbVie: EVENT IS MORE LIKELY RELATED TO STRESS RELATED MUCOSAL DISEASE FROM RESPIRATORY FAILURE SECONDARY TO BILATERAL PULMONARY EMBOLISM AND CARDIAC ARREST.

Event of VENTRICULAR FIBRILLATION

- Investigator: NOT APPLICABLE

- AbbVie: EVENT MORE LIKELY RELATED TO BILATERAL PULMONARY EMBOLI AND ACUTE HYPOXIC RESPIRATORY FAILURE.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** No acute pulmonary disease, minimal platelike volume loss in the lingula

[redacted] **20[redacted] CHEST X-RAY:** Cardiomegaly, increasing left retrocardiac consolidation

[redacted] 20[redacted] **CHEST X-RAY:** Persistent left retrocardiac opacity, may represent atelectasis versus infiltrate, small bilateral pleural effusions, stable position of line and tubes

[redacted] 20[redacted] **COLONOSCOPY:** hemorrhoids, diverticulosis, ulcers in distal rectum, no bleeding

[redacted] 20[redacted] **CT ANGIOGRAM:** Pulmonary arterial emboli, bilateral lower lobe lung interstitial and airspace opacities which may be secondary to PE or pneumonitis, fluid level within the right lower lobebronchus, coronary artery calcifications, spinal scoliosis and degenerative disease

[redacted] 20[redacted] **CT SCAN HEAD:** Mild small vessel ischemic changes in supratentorial white matter, no evidence for acute intracranial injury or abnormality

[redacted] 20[redacted] **EKG:** SINUS RHYTHM WITH CHANGES SUGGESTIVE OF LEFT VENTRICULAR HYPERTROPHY WITH QRS WIDENING, T WAVE ABNORMALITY, CONSIDER ANTERIOR ISCHEMIA

[redacted] 20[redacted] **HEMOGLOBIN:** 11.9 no unit

[redacted] 20[redacted] **MICOBACTERIOLOGY:** Moderate growth normal endogenous flora present

[redacted] 20[redacted] **UPPER GI ENDOSCOPY:** moderate severe esophagitis, with no bleeding

[redacted] 20[redacted] **URINE CULTURE:** No growth

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
蜂巣炎	X			X

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 30 mg QD	5[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: IRRITABLE BOWEL DISEASE	19[redacted]
DEPRESSION: STABLE	20[redacted]
COGNITIVE OR PSYCHIATRIC DISORDER: ANXIETY DISORDER	20[redacted]
DEGENERATIVE DISC DISEASE: C5-6 C6-7	20[redacted]
OTHER: GANGLION CYST	20[redacted]

Prior Procedures	Procedure Year
SURGERY: FUSED RIGHT WRIST	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2 - 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 400	232
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 401	[redacted]20[redacted] / 653	253

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	1000 mg	QD	Y-M: 20[redacted]
IBUPROFEN	600 mg	PRN	Y-M: 20[redacted]
ETANERCEPT	50 mg	OTHER: TWICE WEEKLY	Y-M: 20[redacted]
RITUXIMAB	1000 mg	OTHER: Q 24 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 653
ERGOCALCIFEROL	1000 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 653
IBUPROFEN	600 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 653
CEFTRIAXONE	1 g	QD	Y-M: 20[redacted] / 449	Y-M: 20[redacted] / 449
CEFALEXIN	500 mg	BID	Y-M: 20[redacted] / 449	Y-M: 20[redacted] / 451
CLINDAMYCIN	2700 mg	QD	Y-M: 20[redacted] / 451	Y-M: 20[redacted] / 451
PIP/TAZO	3375 g	QD	Y-M: 20[redacted] / 451	Y-M: 20[redacted] / 452
VANCOMYCIN	1250 mg	QD	Y-M: 20[redacted] / 451	Y-M: 20[redacted] / 453
CEFAZOLIN	2 g	QD	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 454
LACTINEX	2 OTHER: TABLET	BID	Y-M: 20[redacted] / 455	Y-M: 20[redacted] / 462
PARACETAMOL	650 mg	OTHER: Q 4 HOURS PRN	Y-M: 20[redacted] / 455	Y-M: 20[redacted] / 463

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	CELLULITIS OF LEFT HAND
Preferred term	蜂巣炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 449
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
[redacted]20[redacted] (RX DAY 451): WOUND NPTST147-WOUND CULTURE: POSITIVE-STAPH AUREUS POSITIVE	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 449): ABSCESS WAS DRAINED. INCISION AND DRAINAGE PROCEDURE: CULTURE WAS SENT AFTER DRAINAGE. POSITIVE RESULT WAS TREATED; [redacted]20[redacted] (RX DAY 451): ULTRASOUND OF LEFT HAND: SHOWED EDEMA; XRAY LEFT HAND: INDICATED SOFT TISSUE SWELLING WITHOUT BONEY EROSION OR AIR IN THE SOFT TISSUE.	
AE Stopped Rx Day	463
Duration of AE	15 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の5[redacted]歳男性であり，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，左手の蜂巣炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は局面型乾癬，乾癬性関節炎，過敏性腸症候群，不安障害，喫煙者（1 日 1 箱を 25 年間），喫煙者（葉巻タバコの使用）及び現飲酒者（1 日 2～4 杯）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted]年[redacted]月[redacted]日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左手の蜂巣炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左手の蜂巣炎は消失した。

被験者は左手の腫脹及び紅斑を発現した。患部は被験者がガングリオン嚢胞を針で破裂させたために感染を来した。被験者は救急治療室を受診した。X 線検査及び超音波検査が行われた。被験者は嚢胞の感染症と診断され，蜂巣炎を発症した。20[redacted] 年 [redacted] 月 [redacted] 日，膿瘍の切除及びドレナージが行われた。20[redacted] 年 [redacted] 月 [redacted] 日，創傷培養の結果は黄色ブドウ球菌陽性であった。投与された薬剤は，抗生物質であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，florenex，ケフレックス，クリンダマイシン，バンコマイシン，ゾシン，セファゾリン，アセトアミノフェン及びセフトリアキソンであった。

The patient's past medications include:

ENBREL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DEPOMEDROL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Cellulitis of hand (10049022) (Cellulitis (10007882)) [v.21.0] [10049022]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

Event of CELLULITIS OF LEFT HAND

- Investigator: Not applicable

- AbbVie: Event is more likely a complication from the subject using a needle to pop the ganglion cyst.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ULTRASOUND:** Edema

[redacted] **20[redacted] WOUND CULTURE:** Positive, Staph aureus positive.

[redacted] **20[redacted] X-RAY:** Left hand: Soft tissue swelling without bony erosion or air in soft tissue.

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
慢性閉塞性肺疾患	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 30 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: CHICKEN POX	19[redacted]
ASTHMA: BRONCHIAL ASTHMA	19
OTHER: LEFT INGUINAL HERNIA	19
OTHER: PLAQUE PSORIASIS	19
HYPOTHYROIDISM	20
OTHER: CATARACT BILATERAL EYES	20
HYPERLIPIDEMIA: STABLE	20
HYPERTENSION	20
DEPRESSION: STABLE	20

Prior Procedures	Procedure Year
SURGERY: LEFT INGUINAL HERNIA SURGERY	19[redacted]
SURGERY: BILATERAL CATARACT SURGERY	20

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 172	172
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 173	[redacted]20[redacted] / 348	176

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MULTIVITAMIN	1 OTHER:	QD	Y-M: 20[redacted]

	TABLET		
LEVOTHYROXINE	150 OTHER: MCG	QD	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]
ATORVASTATIN	80 mg	QD	Y-M: 20[redacted]
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]
METOPROLOL	50 mg	QD	Y-M: 20[redacted]
RAMIPRIL	10 mg	QD	Y-M: 20[redacted]
PAROXETINE	30 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	700 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]-[redacted]
USTEKINUMAB	90 mg	OTHER: EVERY 12 WEEKS	Y-M: 20[redacted]-[redacted]
IXEKIZUMAB	80 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]-[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
LEVOTHYROXINE	150 OTHER: MCG	QD	Y-M: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	ONGOING
ATORVASTATIN	80 mg	QD	Y-M: 20[redacted]	ONGOING
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]	ONGOING
METOPROLOL	50 mg	QD	Y-M: 20[redacted]	ONGOING
RAMIPRIL	10 mg	QD	Y-M: 20[redacted]	ONGOING
PAROXETINE	30 mg	QD	Y-M: 20[redacted]	ONGOING
SALBUTAMOL	2 OTHER: PUFFS	OTHER: Q 6 HOURS	Y-M: 20[redacted] / 348	ONGOING
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 364
METHYLPREDNISOLONE	40 mg	OTHER: Q 8 HOURS	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 365
PREDNISONE	60 mg	QD	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 366
BENZONATATE	100 mg	TID	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 368
COMBIVENT	3 mL	QID	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 368
GABAPENTIN	300 mg	TID	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 368
HEPARIN	5000 OTHER: UNITS	OTHER: Q 8 HOURS	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 368
VALACICLOVIR	1000 mg	OTHER: Q 8 HOURS	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 381
OXYCOCET	1 OTHER: TABLET	QID	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 392
AZITHROMYCIN	25 mg	QD	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 368
PREDNISONE	50 mg	QD	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 369
GABAPENTIN	300 mg	QD	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 393
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 370	Y-M: 20[redacted] / 372
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 373	Y-M: 20[redacted] / 375
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 376	Y-M: 20[redacted] / 378
PREDNISONE	10 mg	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] /

379 381

Event #2: Serious Adverse Event

Event Description	CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATION
Preferred term	慢性閉塞性肺疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 364 (16 DAYS AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 364): CHEST X-RAY: FINDINGS OF EXACERBATION OF COPD	
AE Stopped Rx Day	368 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PATIENT HAD PREVIOUS HISTORY OF BRONCHIAL ASTHMA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Subject Number: [redacted]

Protocol Number: [redacted]

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，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，慢性閉塞性肺疾患増悪の事象を発現した。

Event 2 の臨床経過：

関連する病歴は気管支喘息，元喫煙者（1 日 3 箱を 30 年間）及び非飲酒者であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は COPD（非重篤な事象）を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は慢性閉塞性肺疾患増悪を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，慢性閉塞性肺疾患増悪は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は息切れ及び咳嗽の増加で入院した。治療が行われ，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，tessalon perle，イプラトロピウム臭化物・アルブテロール硫酸塩（duoneb）合剤，ソル・メドロール，prednisone 及びアジスロマイシンであった。

The patient's past medications include:

REMICADE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

STELARA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IXEKIZUMAB for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Chronic obstructive pulmonary disease exacerbation (10077773) (Chronic obstructive pulmonary disease (10009033)) [v.22.0] [10077773]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATION

- Investigator: PATIENT HAD PREVIOUS HISTORY OF BRONCHIAL ASTHMA

- AbbVie: EVENT IS NOT CONSISTENT WITH THE STUDY DRUG'S MECHANISM OF ACTION. EVENT IS MORE LIKELY RELATED TO SUBJECT'S 90 PACK YEAR SMOKING HISTORY.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] CHEST X-RAY:** Findings of exacerbation of COPD.

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
肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: CHICKEN POX	19[redacted]
ASTHMA	19
OTHER: ENDOMETRIOSIS	19
OTHER: APPENDICITIS	19
MIGRAINE HEADACHE	19
OTHER: ANXIETY DISORDER	19
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20
OTHER: ALLERGIC RHINITIS	20
HYPOTHYROIDISM	20
OTHER: LEFT WRIST FRACTURE	20
OTHER: PLAQUE PSORIASIS	20
NEPHROLITHIASIS	20
OTHER: URINARY INCONTINENCE	20
GASTROESOPHAGEAL REFLUX DISEASE	20
HYPERLIPIDEMIA: STABLE	20
OTHER: LUMBAR THIRD VERTEBRA FRACTURE	20
OTHER: DIVERTICULOSIS	20
HYPERTENSION	20
OSTEOPOROSIS	20
EYE DISEASE/DISORDER: RIGHT EYE CATARACT	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TOTAL HYSTERECTOMY	19[redacted]
SURGERY: APPENDECTOMY	19[redacted]
SURGERY: REPAIR OF LEFT WRIST DUE TO FRACTURE	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 177	177
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 178	[redacted]20[redacted] / 396	219
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 397	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SALBUTAMOL	2.5/3 OTHER: MG/ML	QD	Y-M: 20[redacted]
LEVOTHYROXINE	125 OTHER: MCG	QD	Y-M: 20[redacted]
BLINDED THERAPY	210 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
IBUPROFEN	600 mg	BID	Y-M: 20[redacted]
PAROXETINE	40 mg	QD	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]
FLUTICASONE	1 OTHER: PUFF	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]
ERGOCALCIFEROL	1000 IU	QD	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted]
TOLTERODINE	2 mg	QD	Y-M: 20[redacted] / -192

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

SALBUTAMOL	2.5/3 OTHER: MG/ML	QD	Y-M: 20[redacted]	Not reported.
LEVOTHYROXINE	125 OTHER: MCG	QD	Y-M: 20[redacted]	Not reported.
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]	Not reported.
IBUPROFEN	600 mg	BID	Y-M: 20[redacted]	Not reported.
PAROXETINE	40 mg	QD	Y-M: 20[redacted]	Not reported.
FLUTICASONE	1 OTHER: PUFF	QD	Y-M: 20[redacted]	Not reported.
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	Not reported.
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]	Not reported.
ERGOCALCIFEROL	1000 IU	QD	Y-M: 20[redacted]	Not reported.
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]	Not reported.
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted]	Not reported.
TOLTERODINE	2 mg	QD	Y-M: 20[redacted] / 192	Not reported.
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 165
ONDANSETRON	4 mg	QD	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 166
SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 168
BUDESONIDE	2 mL	BID	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 170
HYDROCODONE	10 mL	QID	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 177
TIOTROPIUM	2.5 mEq	QD	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 178
CEFTRIAXONE	1 mg/kg	QD	Y-M: 20[redacted] / 166	Y-M: 20[redacted] / 170
LEVOFLOXACIN	750 mg	QD	Y-M: 20[redacted] / 166	Y-M: 20[redacted] / 170
METHYLPREDNISOLONE	2 mg	QD	Y-M: 20[redacted] / 166	Y-M: 20[redacted] / 170
COMBIVENT	3 mL	QID	Y-M: 20[redacted] / 166	Y-M: 20[redacted] / 178
INSULIN LISPRO	0.5-1 IU	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 170
PREDNISONE	60 mg	QD	Y-M: 20[redacted] / 170	Y-M: 20[redacted] / 174
CEFUROXIME	500 mg	QD	Y-M: 20[redacted] / 170	Y-M: 20[redacted] / 176
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / 170	Y-M: 20[redacted] / 178

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 165

Age at AE Onset	6[redacted]

Laboratory Testing
[redacted]20[redacted] (RX DAY 166): Erythrocytes: 4.2 [4.2 - 5.4] 10^12/L; Leukocytes: 6.3 [4.8 - 10.8] 10^9/L

Microbiology
[redacted]20[redacted] (RX DAY 165): BLOOD NPTST022-BLOOD CULTURE: NEGATIVE; [redacted]20[redacted] (RX DAY 167): URINE NPTST085-LEGIONELLA AG, URINE: NEGATIVE; URINE NPTST108-PNEUMONIA ANTIGENS, URINE: NEGATIVE

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 165): CHEST X-RAY: PROGRESSING LEFT LUNG CONSOLIDATION;
20[redacted] (RX DAY 167): CHEST XRAY: PROGRESSING LEFT LUNG CONSOLIDATION;
20[redacted] (RX DAY 170): CHEST XRAY: NTERVAL DECREASE IN LEFT LUNG CONSOLIDATION WITH INDICATION OF RESOLVING PNEUMONIA

AE Stopped Rx Day	178
Duration of AE	14 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，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，肺炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は喘息，元喫煙者（1 日 1 箱を 14 年間），アレルギー性鼻炎，肺気腫／慢性閉塞性肺疾患，甲状腺機能低下症，乾癬性関節炎，胃食道逆流性疾患，高血圧及び禁酒であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎は消失した。

被験者は悪心，嘔吐，下痢，発熱及び黄色痰を伴う湿性咳嗽を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，肺炎と診断された。20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで，慢性閉塞性肺疾患の急性増悪（非重篤）も認められた。さらに，非重篤な下痢，嘔吐及び高血糖症も認められたが，これらはいずれも 20[redacted] 年 [redacted] 月 [redacted] 日に消失した。高血糖症は Prednisone 投与によるものであった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，levofloxin，セフトリアキソン，セフロキシム，hycodan 及び prednisone であった。

The patient's past medications include:

BRODALUMAB for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENBREL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

OTEZLA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.22.0] [10035664]

Causality as per reporter (Drug/Vaccine): 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 PNEUMONIA

- Investigator: Not applicable

- AbbVie: Risk factors include advanced age, pre-existing emphysema/chronic obstructive pulmonary disease, and pre-existing gastroesophageal reflux disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD CULTURE:** NEGATIVE

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

[redacted] **20[redacted] CHEST X-RAY:** Progressing Left lung consolidation

[redacted] **20[redacted] CHEST X-RAY:** Progressing Left lung consolidation

[redacted] **20[redacted] CHEST X-RAY:** Interval decrease in left lung consolidation with indication of resolving pneumonia

[redacted] **20[redacted] CXR:** LEFT LOWER LOBE PNEUMONIA

[redacted] **20[redacted] RBC:** 4.19 X10**6/MCL (normal 4.20 to 5.40)

[redacted] **20[redacted] URINE:** LEGIONELLA ANTIGEN: NEGATIVE STREPTOCOCCUS ANTIGEN: NEGATIVE

[redacted] **20[redacted] URINE:** PNEUMONIA ANTIGENS: NEGATIVE

[redacted] **20[redacted] WBC:** 6.3 X10**3/MCL (normal 4.8 to 10.8)

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
腓骨骨折	X			
肋骨骨折	X			
交通事故	X			
肋骨骨折			X	
外傷性血胸	X		X	

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 15 mg QD	7[redacted]	MALE	WHITE

Medical History	Onset Year
EYE DISEASE/DISORDER: MYOPIA	19[redacted]
OTHER: INSOMNIA	19
OBESITY	19
OSTEOARTHRITIS	19
OTHER: SPINAL STENOSIS	19
HYPERTENSION	19
PERIPHERAL NERVE DISORDER: NEUROPATHY	19
CORONARY ARTERY DISEASE: PERCUTANEOUS CORONARY INTERVENTION	19
OTHER: PLAQUE PSORIASIS	19
OTHER: LOW TESTOSTERONE	20
OTHER: CHRONIC BACK PAIN	20
EYE DISEASE/DISORDER: KERATOCONUS	20
EYE DISEASE/DISORDER: BILATERAL CATARACTS	20
KIDNEY DISORDER: CHRONIC KIDNEY DISEASE	20
HYPERLIPIDEMIA: HYPERCHOLESTEROLEMIA	20
DRUG ALLERGIES/REACTIONS: ENBREL - SKIN BOILS	20
OTHER: DECOMPRESSIVE LAMINECTOMY	20
SLEEP APNEA	20
BENIGN PROSTATIC HYPERPLASIA	20
OTHER: ERECTILE DYSFUNCTION	20
OTHER: PROSTATITIS	20

Prior Procedures	Procedure Year
SURGERY: VASECTOMY	19[redacted]
SURGERY: KNEE ARTHROPLASTY RIGHT	19[redacted]
SURGERY: KNEE ARTHROPLASTY LEFT	20[redacted]
SURGERY: CATARACTS REMOVAL	20[redacted]
SURGERY: STENT PLACEMENT	20[redacted]
SURGERY: STENT X2	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 14	14

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 19[redacted]
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 19[redacted]
CO-DIOVAN	320/25 mg	QD	Y-M: 20[redacted]
PIOGLITAZONE	30 mg	QD	Y-M: 20[redacted]
DIPHENHYDRAMINE	50 mg	QD	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
ROSUVASTATIN	20 mg	QD	Y-M: 20[redacted]
TRAMADOL	50 mg	OTHER: 2 Q AM / 4 Q PM	Y-M: 20[redacted]
CELECOXIB	200 mg	QD	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY WEEK	Y-M: 20[redacted]
KRILL OIL	500 mg	QD	Y-M: 20[redacted]
TEMAZEPAM	30 mg	QD	Y-M: 20[redacted]
TICAGRELOR	60 mg	BID	Y-M: 20[redacted]
TESTOSTERONE	6 OTHER: PELLETS	OTHER: Q 3 MONTHS	Y-M: 20[redacted]
GABAPENTIN	800 mg	TID	Y-M: 20[redacted]
TADALAFIL	5 mg	QD	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted] / -303

DULOXETINE	50 mg	QD	Y-M: 20[redacted]-[redacted] / -242
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]-[redacted] / -150

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
MULTIVITAMIN	1 OTHER: TABLET	QD	Y-M: 19[redacted]	Y-M: 20[redacted]-[redacted] / 16
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 19[redacted]	Y-M: 20[redacted]-[redacted] / 16
CO-DIOVAN	320/25 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
PIOGLITAZONE	30 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
DIPHENHYDRAMINE	50 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
ROSUVASTATIN	20 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
TRAMADOL	50 mg	OTHER: 2 Q AM / 4 Q PM	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
KRILL OIL	500 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
TEMAZEPAM	30 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
TICAGRELOR	60 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
TESTOSTERONE	6 OTHER: PELLETS	OTHER: Q 3 MONTHS	Y-M: 20[redacted]-[redacted]	Y-M: 20[redacted]-[redacted] / 16
GABAPENTIN	800 mg	TID	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
TADALAFIL	5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted]-[redacted] / 16
DULOXETINE	50 mg	QD	Y-M: 20[redacted]-[redacted] / -242	Y-M: 20[redacted]-[redacted] / 16
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]-[redacted] / -150	Y-M: 20[redacted]-[redacted] / 16
OXYCODONE	10 mg	BID	Y-M: 20[redacted]-[redacted] / 5	Y-M: 20[redacted]-[redacted] / 16

Event #1: Serious Adverse Event

Event Description	LEFT FIBULAR FRACTURE
Preferred term	腓骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 5

Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 7): SURGERY ON FIBULAR FRACTURE: RESOLVING	
AE Stopped Rx Day	16 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CAR CRASH
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #2: Serious Adverse Event

Event Description	RIGHT FRACTURED RIBS
Preferred term	肋骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 5
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 7): SURGERY ON FIBULAR FRACTURE: RESOLVING	
AE Stopped Rx Day	16 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CAR CRASH
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	MOTOR VEHICLE ACCIDENT
Preferred term	交通事故
AE Onset Date / Rx Day	[redacted]20[redacted] / 5
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 7): SURGERY ON FIBULAR FRACTURE: RESOLVING	
AE Stopped Rx Day	5
Duration of AE	1 DAY
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, PERSIST OR SIGNIF DISABILITY/INCAPACITY, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #4: Serious Adverse Event, Death

Event Description	RIGHT HEMOTHORAX SECONDARY TO RIB FRACTURES
Preferred term	肋骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 16 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 7): SURGERY ON FIBULAR FRACTURE: RESOLVING

AE Stopped Rx Day	16 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	1 DAY
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RIGHT HEMOTHORAX SECONDARY TO RIB FRACTURES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	RESULTS IN DEATH

Event #5: Serious Adverse Event, Death

Event Description	RIGHT HEMOTHORAX SECONDARY TO RIB FRACTURES
Preferred term	外傷性血胸
AE Onset Date / Rx Day	[redacted]20[redacted] / 16 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 7): SURGERY ON FIBULAR FRACTURE: RESOLVING

AE Stopped Rx Day	16 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	1 DAY
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RIGHT HEMOTHORAX SECONDARY TO RIB FRACTURES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	RESULTS IN DEATH

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，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，左腓骨骨折，右肋骨骨折，自動車事故及び肋骨骨折による致死的な右血胸の事象を発現した。

Event 1～5 の臨床経過：

関連する病歴は肥満，変形性関節症，高血圧，ニューロパチー，経皮的冠インターベンション，局面型乾癬，乾癬性関節炎，高コレステロール血症，睡眠時無呼吸，ステント留置（ステント 2 ヵ所），非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左腓骨骨折，右肋骨骨折及び自動車事故を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，自動車事故は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肋骨骨折による右血胸を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死因は肋骨骨折による右血胸と報告された。剖検が実施された。

被験者の趣味はカーレースであった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は自動車事故により左腓骨及び右肋骨を骨折した。同日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，左腓骨の手術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は自宅で死亡した。20[redacted] 年 [redacted] 月 [redacted] 日，剖検により，死因は肋骨骨折による右血胸と報告された。

投与された薬剤はオキシコドンであった。

The patient's past medications include:

PREDNISONE for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

CELEBREX for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

HUMIRA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COSENTYX for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Rib fracture (10039117) (Rib fracture (10039117)) [v.21.0] [10039117]

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

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

Dechallenge: Not Applicable

2) Traumatic hemothorax (10074504) (Traumatic haemothorax (10074487)) [v.21.0] [10074504]

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

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

Dechallenge: Not Applicable

3) Fibula fracture (10016667) (Fibula fracture (10016667)) [v.21.0] [10016667]

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

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

Dechallenge: Not Applicable

4) Fractured ribs (10017307) (Rib fracture (10039117)) [v.21.0] [10017307]

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

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

Dechallenge: Not Applicable

5) Motor vehicle accident (10028008) (Road traffic accident (10039203)) [v.21.0] [10028008]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of RIGHT HEMOTHORAX SECONDARY TO RIB FRACTURES

- Investigator: RIGHT HEMOTHORAX SECONDARY TO RIB FRACTURES

- AbbVie: Event is more likely related to trauma from a motor vehicle accident.

Event of LEFT FIBULAR FRACTURE

- Investigator: CAR CRASH

- AbbVie: EVENT IS AN ACCIDENTAL INJURY RESULTING FROM CAR ACCIDENT.

Event of RIGHT FRACTURED RIBS

- Investigator: CAR CRASH

- AbbVie: EVENT IS AN ACCIDENTAL INJURY RESULTING FROM CAR ACCIDENT.

Event of MOTOR VEHICLE ACCIDENT

- Investigator: UNKNOWN

- AbbVie: EVENT IS MORE LIKELY SECONDARY TO TRAUMATIC ACCIDENTAL EVENT.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** Findings were normal. Calcified granulomas, pleural scarring, and pleural thickening absent. No signs of active TB. Finding not indicative of previous TB infection.

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Normal

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 69 MM/HR

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 62 MM/HR

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
直腸腺癌	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	6[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
OTHER: MEASLES	19[redacted]
OTHER: MUMPS	19
OTHER: CHICKEN POX	19
OTHER: CARDIAC MURMUR	19
ANEMIA: NOT ON ANY TREATMENT	19
OTHER: POST-MENOPAUSAL	19
OTHER: PLAQUE PSORIATIC ARTHRITIS	20
OTHER: VITAMIN D DEFICIENCY	20
OTHER: LEFT SHOULDER PAIN	20
DRUG ALLERGIES/REACTIONS: TETRACYCLINE HCL	20
OTHER: LOW BACK PAIN	20
OTHER: DIFFUSE ANTHROPATHY OF THE FACETS AT THE MED TO LOWER LUMBER SPINE	20
EYE DISEASE/DISORDER: DRY EYES	20
HYPERLIPIDEMIA: SUBJECT IS TAKING ATORVASTATIN	20
HYPERTENSION	20
OTHER: HEADACHES	20
OTHER: INSOMNIA	20
OTHER: LOCALIZED EDEMA	20
ANGINA	20
CORONARY ARTERY DISEASE: N/A	20
OTHER: NON-ST ELEVATION MYOCARDIAL INFARCTION	20
OSTEOPOROSIS	20

Prior Procedures	Procedure Year
SURGERY: CORONARY ARTERY BYPASS GRAFT	20[redacted]
SURGERY: LEFT HEART CATHETERIZATION	20

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETANERCEPT	50 OTHER: MG/ML	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
FOLIC ACID	400 OTHER: MCG	QD	Y-M: 20[redacted]
MELOXICAM	15 mg	QD	Y-M: 20[redacted]
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
ATORVASTATIN	40 mg	QD	Y-M: 20[redacted]
FUROSEMIDE	40 mg	QD	Y-M: 20[redacted]
METOPROLOL	25 mg	BID	Y-M: 20[redacted]
POTASSIUM	10 mEq	QD	Y-M: 20[redacted]
UBIDECARENONE	1 OTHER: CAP	QD	Y-M: 20[redacted]
PREDNISONE	2 mg	OTHER: QHS	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]
COLECALCIFEROL	2 OTHER: TABS	QD	Y-M: 20[redacted]
ALENDRONIC ACID	70 mg	EVERY WEEK	Y-M: 20[redacted] / -276

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	400 OTHER: MCG	QD	Y-M: 20[redacted]	ONGOING
MELOXICAM	15 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 218
ATORVASTATIN	40 mg	QD	Y-M: 20[redacted]	ONGOING
FUROSEMIDE	40 mg	QD	Y-M: 20[redacted]	ONGOING
METOPROLOL	25 mg	BID	Y-M: 20[redacted]	ONGOING
POTASSIUM	10 mEq	QD	Y-M: 20[redacted]	ONGOING
UBIDECARENONE	1 OTHER: CAP	QD	Y-M: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	2 OTHER: TABS	QD	Y-M: 20[redacted]	ONGOING
ALENDRONIC ACID	70 mg	EVERY WEEK	Y-M: 20[redacted] / 276	ONGOING
AXOTAL	50/325/40 mg	PRN	Y-M: 20[redacted] / 153	Y-M: 20[redacted] / 154
IRON	325 mg	QD	Y-M: 20[redacted] / 218	ONGOING
CAPECITABINE	1650 mg	QD	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 278

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

Event Description	MODERATELY DIFFERENTIATED INVASIVE ADENOCARCINOMA (RECTUM)
Preferred term	直腸腺癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 153
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 153): BIOPSY: COLON, CECUM, BIOPSY - ACUTE COLITIS, NO VIRAL INCLUSIONS OR PARASITES, NO DYSPLASIA OR MALIGNANCY, OR NO SIGNIFICANT ARCHITECTURAL DISTORTION OR GRANULOMAS; BIOPSY: COLON RECTUM POLPY BIOPSY - TUBULAR ADENOMA; BIOPSY: COLON SIGMOID POLYP BIOPSY, - TUBULAR ADENOMA; BIOPSY: COLON, TRANSVERSE POLYP X 2, BIOPSY - HYPERPLASTIC POLYP; COLONOSCOPY: LOCALIZED MILD INFLAMMATION WAS FOUND IN THE CECUM SECONDARY TO COLITIS. ONE 6 MM POLYP IN THE TRANSVERSE COLON, REMOVED WITH A HOT SNARE. TWO 6 TO 7 MM POLYPS IN THE DESCENDING COLON, REMOVED WITH A; PATHOLOGY - COLON, RECTUM, MALIGNANT APPEARING MASS, BIOPSY: MODERATELY DIFFERENTIATED INVASIVE ADENOCARCINOMA; [redacted]20[redacted] (RX DAY 196): PET SCAN: FLUORODEOXYGLUCOSE AVID MASS AT THE RECTOSIGMOID JUNCTION C/W KNOWN PRIMARY MALIGNANCY; [redacted]20[redacted] (RX DAY 210): MRI PELVIS WITH ULTRASOUND: CIRCUMFERENTIAL RECTAL LESION, APPROXIMATELY 3.5COM LONG. LOWER MARGIN APPROXIMATE 9-10 CM ABOVE ANUS WELL ABOVE THE SPHINCTER. LESION EXTENDS THROUGH LAMINA PROPRIA INTO PERINEURAL FAT. SINGLE 7MM NO; [redacted]20[redacted] (RX DAY 334): ROBOTIC LOW ANTERIOR RESECTION OF THE RECTUM AND COVERING ILEOSTOMY: RECTUM REMOVED. ANASTOMOSIS WAS LOW AND THE PATIENT HAD RADIATION THERAPY RECENTLY, AN ILEOSTOMY WAS CREATED.

AE Stopped Rx Day	491 (323 DAYS AFTER LAST TREATMENT)
Duration of AE	339 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の6[redacted]歳女性であり，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，中分化型浸潤腺癌（直腸）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は元喫煙者（1 日 1 箱を 10 年間），閉経後，局面型乾癬性関節炎，乾癬性関節炎，現飲酒者（1 日 2 杯未満）及び乳癌の家族歴（姉妹 2 人）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は中分化型浸潤腺癌（直腸）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，中分化型浸潤腺癌（直腸）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は年齢を考慮して初めて結腸内視鏡検査を受けた。直腸近位部で葉状体様／絨毛状で非閉塞性の，中程度の大きさの腫瘤が見つかり，生検が行われた。病理診断の結果，中分化型浸潤腺癌であった。報告されたその他の所見は，大腸炎による盲腸の限局性炎症（非重篤）及び非出血性内痔核（非重篤）であった。本事象により治験薬の投与が完全に中止された。20[redacted] 年 [redacted] 月，化学療法が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は慢性の失血による鉄欠乏性貧血（非重篤）を発現し，硫酸鉄水和物が投与された。20[redacted] 年 [redacted] 月 [redacted] 日，持続的な直腸出血（非重篤）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，直腸のロボット支援低位前方切除術及び予防的回腸瘻造設術が行われた。直腸は切除された。放射線療法が行われた。20[redacted] 年 [redacted] 月 [redacted] 日現在，化学療法は完了している。被験者は安定状態にあり，担当腫瘍内科医によれば，被験者は寛解にあった。

投与された薬剤はカペシタビンであった。

Causality for ABT-494 (Blinded)

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1) Rectal adenocarcinoma (10038019) (Rectal adenocarcinoma (10038019)) [v.21.1] [10038019]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of MODERATELY DIFFERENTIATED INVASIVE ADENOCARCINOMA (RECTUM)

- Investigator: Not applicable

- AbbVie: Risk factors include the patient's age and obesity.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BIOPSY:** COLON, TRANSVERSE POLYP X 2, BIOPSY - HYPERPLASTIC POLYP; COLON SIGMOID POLYP BIOPSY, - TUBULAR ADENOMA; COLON RECTUM POLPY BIOPSY - TUBULAR ADENOMA; COLON, CECUM, BIOPSY - ACUTE COLITIS, NO VIRAL INCLUSIONS OR PARASITES, NO DYSPLASIA OR MALIGNANCY, OR NO SIGNIFICANT ARCHITECTURAL DISTORTION OR GRANULOMAS

[redacted] **20[redacted] COLONOSCOPY:** LOCALIZED MILD INFLAMMATION WAS FOUND IN THE CECUM SECONDARY TO COLITIS. ONE 6 MM POLYP IN THE TRANSVERSE COLON, REMOVED WITH A HOT SNARE. TWO 6 TO 7 MM POLYPS IN THE DESCENDING COLON, REMOVED WITH A COLD BIOPSY FORCEPS. ONE 7 MM POLYP IN THE SIGMOID COLON, REMOVED WITH A HOT SNARE. ONE 7 MM POLYP AT THE RECTO-SIGMOID COLON, REMOVED WITH A HOT SNARE. LIKELY MALIGNANT TUMOR IN THE PROXIMAL RECTUM, BIOPSIED. THE EXAMINED PORTION OF THE ILEUM WAS NORMAL. THE EXAMINATION WAS OTHERWISE NORMAL.

[redacted] **20[redacted] MRI PELVIS:** CIRCUMFERENTIAL RECTAL LESION, APPROXIMATELY 3.5CM LONG. LOWER MARGIN APPROXIMATE 9-10 CM ABOVE ANUS WELL ABOVE THE SPHINCTER. LESION EXTENDS THROUGHLAMINA PROPRIA INTO PERINEURAL FAT. SINGLE 7MM NODE IDENTIFIED IN THE PERIRECTAL SPACE. CRM IS INTACT. LESION IS MINIMALLY 7MM FROM THE RIGHT SIDE OF THE CRM.

[redacted] **20[redacted] PATHOLOGY - COLON, RECTUM, MALIGNANT APPEARING MASS, BIOPSY:** MODERATELY DIFFERENTIATED INVASIVE ADENOCARCINOMA.

[redacted] **20[redacted] PET SCAN:** fluorodeoxyglucose avid mass at the rectosigmoid junction c/w known primary malignancy

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
失血性貧血	X			X
出血性十二指腸潰瘍	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
GASTROINTESTINAL BLEED: BLOOD IN THE STOOL	20
OTHER: TINEA CRURIS	20
OTHER: ABNORMAL EKG	20
OTHER: SHORTNESS OF BREATH	20
OBESITY	20
OTHER: ARTHRITIC CHANGES IN THE FIRST CARPOMETACARPAL JOINT AND THE FIRST INTERPHALANGEAL JOINT	20
OTHER: ARTHRITIC CHANGES ON THE FIRST METATARSOPHALANGEAL ARTICULATION	20
OTHER: MARGINAL EROSION OF THE HEAD OF THE FIRST METATARSAL	20
OTHER: MILD PERIARTICULAR SOFT TISSUE SWELLING BY 2ND AND 3RD PROXIMAL INTERPHALANGEAL JOINTS	20
OTHER: OSTEOPHYTE LOWER THORACIC SPINE	20
OTHER: SNORING	20

Prior Procedures	Procedure Year
SURGERY: DEVIATED SEPTUM SURGERY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 394	226
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 395	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40/0.8 OTHER: MG/ML	EVERY 2 WEEKS	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
NAPROXEN	220 mg	PRN	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PREDNISONE	5 mg	QD	Y-M: 20[redacted]	Not reported.
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	Not reported.
NAPROXEN	220 mg	PRN	Y-M: 20[redacted]	Not reported.
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]	Not reported.
ANTIVIRALS FOR SYSTEMIC USE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 408	Y-M: 20[redacted] / 408
NALOXONE	0.2 mg	PRN	Y-M: 20[redacted] / 419	Y-M: 20[redacted] / 420
VANCOMYCIN	1250 mg	OTHER: Q12H	Y-M: 20[redacted] / 419	Y-M: 20[redacted] / 420
BLOOD AND RELATED PRODUCTS	6 OTHER: UNITS	PRN	Y-M: 20[redacted] / 419	Y-M: 20[redacted] / 421
DOCUSATE	100 mg	PRN	Y-M: 20[redacted] / 419	Y-M: 20[redacted] / 422
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 419	Y-M: 20[redacted] / 422
SODIUM CHLORIDE	75 mL	OTHER: 75 ML/HR COUNTINUOUS	Y-M: 20[redacted] / 419	Y-M: 20[redacted] / 422
HYDROCORTISONE	50 mg	OTHER: Q12H	Y-M: 20[redacted] / 420	Y-M: 20[redacted] / 422
MELATONIN	3 mg	QD	Y-M: 20[redacted] / 420	Y-M: 20[redacted] / 422
ONDANSETRON	4 mg	OTHER: Q8H	Y-M: 20[redacted] / 420	Y-M: 20[redacted] / 422
PANTOPRAZOLE	8 mg	OTHER: CONTINUOUS IV PRN	Y-M: 20[redacted] / 420	Y-M: 20[redacted] / 422
TRAMADOL	25 mg	TID	Y-M: 20[redacted] / 420	Y-M: 20[redacted] / 422
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 422	Not reported.

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	ACUTE BLOOD LOSS ANEMIA
Preferred term	失血性貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 419
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 419): Albumin: 34 [35 - 50] g/L; Blood Urea Nitrogen: 17.49 [2.86 - 8.57] mmol/L; Chloride: 111 [99 - 109] mmol/L; Erythrocytes: 2.4 [4.4 - 6] 10^12/L; Glucose: 9.88 [3.61 - 5.5] mmol/L; Hematocrit: 0.22 [0.41 - 0.51] fraction of 1; Hematocrit: 0.26 [0.41 - 0.51] fraction of 1; Hemoglobin: 81 [140 - 180] g/L; Hemoglobin: 70 [140 - 180] g/L; Leukocytes: 14.3 [4.5 - 11] 10^9/L; NPTST040-CO2: 18 [24 - 31] mEq/L; NPTST055-D-DIMER: 0.85 [0 - 0.4] UG/ML FEU; NPTST075-IMMATURE GRANULOCYTES: 1.5

[0 - 1] %; NPTST078-IRON BINDING CAPACITY: 222 [260 - 460] ug/dL; NPTST079-IRON BINDING CAPACITY % SATURAT: 52.7 [20 - 40] %; NPTST084-LDH: 291 [300 - 600] U/L; NPTST090-MCV: 104.5 [82 - 100] fL; NPTST110-PROTHROMBIN TIME: 14.7 [11.5 - 14.5] sec; NPTST117-RDW - SD: 58.3 [37 - 55] fL; NPTST120-RETICULOCYTE % AUTO: 2.3 [0.5 - 2.1] %; Protein: 55 [63 - 82] g/L; [redacted]20[redacted] (RX DAY 420): Erythrocytes: 2.3 [4.4 - 6] 10^12/L; Glucose: 12.1 [3.61 - 5.5] mmol/L; Hematocrit: 0.23 [0.41 - 0.51] fraction of 1; Hematocrit: 0.23 [0.41 - 0.51] fraction of 1; Hemoglobin: 76 [140 - 180] g/L; Hemoglobin: 76 [140 - 180] g/L; Leukocytes: 11.6 [4.5 - 11] 10^9/L; NPTST118-RDW-SD: 59.7 [37 - 55] fL; [redacted]20[redacted] (RX DAY 421): Blood Urea Nitrogen: 11.78 [2.86 - 8.57] mmol/L; Glucose: 8.88 [3.61 - 5.5] mmol/L; Hematocrit: 0.23 [0.41 - 0.51] fraction of 1; Hematocrit: 0.25 [0.41 - 0.51] fraction of 1; Hematocrit: 0.25 [0.41 - 0.51] fraction of 1; Hemoglobin: 83 [140 - 180] g/L; Hemoglobin: 76 [140 - 180]

Microbiology

[redacted]20[redacted] (RX DAY 419): URINE NPTST047-CULTURE: NEGATIVE; BLOOD NPTST048-CULTURE AEROBIC AND ANAEROBIC: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 419): CHEST X-RAY: 1. THE LUNGS ARE CLEAR OF ACUTE INFILTRATE, CONSOLIDATION, OR PLUERAL EFFUSION. 2. THE CARDIAC SILHOUETTE IS NOT ENLARGED. PULMONARY VASCULATURE IS WITHIN NORMAL LIMITS. THE THORACIC AORTA IS ATHEROS; CT ABDOMEN PELVIS WO CONTRAST: INDETERMINATE DEBRIS AND SIMPLE FLUID IN THE STOMACH, HIGHER DENSITY NOTED POSTERIORLY. NO DEFINITE ACUTE GI BLEEDING IS IDENTIFIED BUT CONSIDER NG TUBE PLACEMENT AND LAVAGE FOR FURTHER EVALUATION. OT; CT HEAD WO CONTRAST: 1. NO CT EVIDENCE OF ACUTE INTRACRANIAL ABNORMALITY; ECG 12 LEAD: NORMAL SINUS RHYTHM-RIGHT BUNDLE BRANCH BLOCK-ABNORMAL ECG; ECHOCARDIOGRAM: LEFT VENTRICULAR FUNCTION IS HYPERDYNAMIC. LEFT VENTRICULAR EJECTION FRACTION IS > 70% NO PERICARDIAL EFFUSION SEEN; O POSITIVE BLOOD TRANSFUSION: 6 UNITS TOTAL BLOOD TRANSFUSION OVER 2 DAYS TO IMPROVE HEMOGLOBIN LEVELS.; US DUPLEX VENOUS LOWER EXTREMITY: NORMAL BILATERAL EXTREMITY VENOUS DOPPLER EXAMINATION. THERE IS NO EVIDENCE OF DEEP VENOUS THROMBOSIS; [redacted]20[redacted] (RX DAY 421): EGD: THE ESOPHAGEAL MUCOSA APPEARED NORMAL. SUBMUCOSAL NODULE NOTED IN THE PROXIMAL BODY AS NOTED YESTERDAY. EROSIONS WERE NOTED AT THE PREVIOUS ANTRAL BIOPSY SITE. 2 ENDOCLIPS WERE PLACED AT THE DUODEN; UPPER GI ENDOSCOPY: NORMAL ESOPHAGUS. HEMATIN IN GASTRIC BODY. BLOOD IN DUODENAL BULB. CHRONIC GASTRITIS. BIOPSIED. ONE OOZING DUODENAL ULCER WITH VISIBLE VESSEL. INJECTED. CLIPS WERE PLACED.

AE Stopped Rx Day	424
Duration of AE	6 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	DUODENAL ULCER BLEEDING
Preferred term	出血性十二指腸潰瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 419
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 419): Albumin: 34 [35 - 50] g/L; Blood Urea Nitrogen: 17.49 [2.86 - 8.57] mmol/L; Chloride: 111 [99 - 109] mmol/L; Erythrocytes: 2.4 [4.4 - 6] 10^12/L; Glucose: 9.88 [3.61 - 5.5] mmol/L;

Hematocrit: 0.22 [0.41 - 0.51] fraction of 1; Hematocrit: 0.26 [0.41 - 0.51] fraction of 1; Hemoglobin: 81 [140 - 180] g/L; Hemoglobin: 70 [140 - 180] g/L; Leukocytes: 14.3 [4.5 - 11] 10^9/L; NPTST040-CO2: 18 [24 - 31] mEq/L; NPTST055-D-DIMER: 0.85 [0 - 0.4] UG/ML FEU; NPTST075-IMMATURE GRANULOCYTES: 1.5 [0 - 1] %; NPTST078-IRON BINDING CAPACITY: 222 [260 - 460] ug/dL; NPTST079-IRON BINDING CAPACITY % SATURAT: 52.7 [20 - 40] %; NPTST084-LDH: 291 [300 - 600] U/L; NPTST090-MCV: 104.5 [82 - 100] fL; NPTST110-PROTHROMBIN TIME: 14.7 [11.5 - 14.5] sec; NPTST117-RDW - SD: 58.3 [37 - 55] fL; NPTST120-RETICULOCYTE % AUTO: 2.3 [0.5 - 2.1] %; Protein: 55 [63 - 82] g/L; [redacted]20[redacted] (RX DAY 420): Erythrocytes: 2.3 [4.4 - 6] 10^12/L; Glucose: 12.1 [3.61 - 5.5] mmol/L; Hematocrit: 0.23 [0.41 - 0.51] fraction of 1; Hematocrit: 0.23 [0.41 - 0.51] fraction of 1; Hemoglobin: 76 [140 - 180] g/L; Hemoglobin: 76 [140 - 180] g/L; Leukocytes: 11.6 [4.5 - 11] 10^9/L; NPTST118-RDW-SD: 59.7 [37 - 55] fL; [redacted]20[redacted] (RX DAY 421): Blood Urea Nitrogen: 11.78 [2.86 - 8.57] mmol/L; Glucose: 8.88 [3.61 - 5.5] mmol/L; Hematocrit: 0.23 [0.41 - 0.51] fraction of 1; Hematocrit: 0.25 [0.41 - 0.51] fraction of 1; Hematocrit: 0.25 [0.41 - 0.51] fraction of 1; Hemoglobin: 83 [140 - 180] g/L; Hemoglobin: 76 [140 - 180]

Microbiology

[redacted]20[redacted] (RX DAY 419): URINE NPTST047-CULTURE: NEGATIVE; BLOOD NPTST048-CULTURE AEROBIC AND ANAEROBIC: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 419): CHEST X-RAY: 1. THE LUNGS ARE CLEAR OF ACUTE INFILTRATE, CONSOLIDATION, OR PLUERAL EFFUSION. 2. THE CARDIAC SILHOUETTE IS NOT ENLARGED. PULMONARY VASCULATURE IS WITHIN NORMAL LIMITS. THE THORACIC AORTA IS ATHEROS; CT ABDOMEN PELVIS WO CONTRAST: INDETERMINATE DEBRIS AND SIMPLE FLUID IN THE STOMACH, HIGHER DENSITY NOTED POSTERIORLY. NO DEFINITE ACUTE GI BLEEDING IS IDENTIFIED BUT CONSIDER NG TUBE PLACEMENT AND LAVAGE FOR FURTHER EVALUATION. OT; CT HEAD WO CONTRAST: 1. NO CT EVIDENCE OF ACUTE INTRACRANIAL ABNORMALITY; ECG 12 LEAD: NORMAL SINUS RHYTHM-RIGHT BUNDLE BRANCH BLOCK-ABNORMAL ECG; ECHOCARDIOGRAM: LEFT VENTRICULAR FUNCTION IS HYPERDYNAMIC. LEFT VENTRICULAR EJECTION FRACTION IS > 70% NO PERICARDIAL EFFUSION SEEN; O POSITIVE BLOOD TRANSFUSION: 6 UNITS TOTAL BLOOD TRANSFUSION OVER 2 DAYS TO IMPROVE HEMOGLOBIN LEVELS.; US DUPLEX VENOUS LOWER EXTREMITY: NORMAL BILATERAL EXTREMITY VENOUS DOPPLER EXAMINATION. THERE IS NO EVIDENCE OF DEEP VENOUS THROMBOSIS; [redacted]20[redacted] (RX DAY 421): EGD: THE ESOPHAGEAL MUCOSA APPEARED NORMAL. SUBMUCOSAL NODULE NOTED IN THE PROXIMAL BODY AS NOTED YESTERDAY. EROSIONS WERE NOTED AT THE PREVIOUS ANTRAL BIOPSY SITE. 2 ENDOCLIPS WERE PLACED AT THE DUODEN; UPPER GI ENDOSCOPY: NORMAL ESOPHAGUS. HEMATIN IN GASTRIC BODY. BLOOD IN DUODENAL BULB. CHRONIC GASTRITIS. BIOPSIED. ONE OOZING DUODENAL ULCER WITH VISIBLE VESSEL. INJECTED. CLIPS WERE PLACED.

AE Stopped Rx Day	421
Duration of AE	3 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUBJECT HAS CHRONIC GASTRITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性であり，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，急性失血性貧血及び出血性十二指腸潰瘍の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は元喫煙者（1 日 1 箱を 11 年間），乾癬性関節炎，血便，息切れ及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性失血性貧血及び出血性十二指腸潰瘍を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，出血性十二指腸潰瘍は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，急性失血性貧血は消失した。

事象発現前，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日にインフルエンザウイルスに感染（非重篤な事象）し，20[redacted] 年 [redacted] 月 [redacted] 日に消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，ベッドで休んでいたとき，突然，全身に寒気を感じ，立ち上がるのが困難となった。やっと立ち上がることができたものの，ベッドの近くで転倒した。トイレに行き，失神した。後頭部を打ち，その後は何も覚えていない。同日，被験者は入院した。被験者は失神，低血圧及び胃炎（いずれも非重篤な事象）を発現した。被験者は悪心，頭部ふらふら感及び黒色タール様便も発現した。被験者は貧血と診断され，血液 6 単位を輸血された。20[redacted] 年 [redacted] 月 [redacted] 日，食道胃十二指腸内視鏡検査（EGD）が行われ，内視鏡クリップが 2 個留置された。翌日，再度 EGD が行われたが，活動性の出血は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は症状なく退院した。

治験責任医師によると，十二指腸潰瘍の既往歴の有無は不明であった。

投与された薬剤は，塩化ナトリウム，タイレノール，ヒドロコルチゾンナトリウム，zofran, pantoprazole，バンコマイシン及びトラマドールであった。

The patient's past medications include:

HUMIRA for PSORIATIC ARTHRITIS (20[redacted] - [redacted] [redacted] 20[redacted])

XOFLUZA for FLU VIRUS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute blood loss anemia (10082299) (Blood loss anaemia (10082297)) [v.22.0] [10082299]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

2) Duodenal ulcer bleeding (10071802) (Duodenal ulcer haemorrhage (10013839)) [v.22.0] [10071802]

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 ACUTE BLOOD LOSS ANEMIA

- Investigator: Not Applicable.

- AbbVie: More likely related to concurrent duodenal ulcer.

Event of DUODENAL ULCER BLEEDING

- Investigator: Subject has chronic gastritis

- AbbVie: Risk factors include long term concomitant use of prednisone, aleve, and methotrexate.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] BUN:** 49 mg/dL (normal 8 to 24)

[redacted] **20[redacted] CHEST X-RAY:** 1. THE LUNGS ARE CLEAR OF ACUTE INFILTRATE, CONSOLIDATION, OR PLUERAL EFFUSION. 2. THE CARDIAC SILHOUETTE IS NOT ENLARGED. PULMONARY VASCULATURE IS WITHIN NORMAL LIMITS. THE THORACIC AORTA IS ATHEROSCLEROTIC. 3. THE VISUALIZED OSSEOUS STRUCTURES ARE INTACT.

[redacted] **20[redacted] CT ABDOMEN PELVIS:** INDETERMINATE DEBRIS AND SIMPLE FLUID IN THE STOMACH, HIGHER DENSITY NOTED POSTERIORLY. NO DEFINITE ACUTE GI BLEEDING IS IDENTIFIED BUT CONSIDER NG TUBE PLACEMENT AND LAVAGE FOR FURTHER EVALUATION. OTHERWISE UNREMARKABLE UNENHANCED CT ABDOMEN PELVIS

[redacted] **20[redacted] CT HEAD:** 1. NO CT EVIDENCE OF ACUTE INTRACRANIAL ABNORMALITY

[redacted] **20[redacted] D-DIMER:** 0.85 MCG/ML (normal 0.0 to 0.4)

[redacted] **20[redacted] ECHO:** LEFT VENTRICULAR FUNCTION IS HYPERDYNAMIC. LEFT VENTRICULAR EJECTION FRACTION IS > 70% NO PERICARDIAL EFFUSION SEEN

[redacted] **20[redacted] EGD:** THE ESOPHAGEAL MUCOSA APPEARED NORMAL. SUBMUCOSAL NODULE NOTED IN THE PROXIMAL BODY AS NOTED YESTERDAY. EROSIONS WERE NOTED AT THE PREVIOUS ANTRAL BIOPSY SITE. 2 ENDOCLIPS WERE PLACED AT THE DUODENAL ULCER. THIS SITE WAS CLEAN WITHOUT ANY EVIDENCE OF BLEEDING. THE DUODENUM WAS EXAMINED UP TO THE THIRD PORTION OF THE DUODENUM. HEALTHY-APPEARING BOWEL WAS PRESENT WITHOUT EVIDENCE OF BLEEDING.

[redacted] **20[redacted] EGD:** REPEAT: NO FURTHER BLEEDING.

[redacted] **20[redacted] EKG:** NORMAL SINUS RHYTHM-RIGHT BUNDLE BRANCH BLOCK-ABNORMAL ECG

[redacted] **20[redacted] GLUCOSE:** 178 mg/dL (normal 65 to 99)

[redacted] **20[redacted] HCT:** 22.9 % (normal 41.0 to 51.0)

[redacted] **20[redacted] HCT:** 25.8 % (normal 41.0 to 51.0)

[redacted] **20[redacted] HGB:** 8.1 G/DL (normal 14.0 to 18.0)

[redacted] **20[redacted] HGB:** 7.6 G/DL (normal 14.0 to 18.0)

[redacted] **20[redacted] HGB:** 8.5 G/DL (normal 14.0 to 18.0)

[redacted] **20[redacted] IRON BINDING CAPACITY:** 222 MCG/DL (normal 260 to 460)

[redacted] **20[redacted] IRON BINDING CAPACITY % SATURATION:** 52.7 % (normal 20 to 40)

[redacted] **20[redacted] RBC:** 2.44 X10**6/MCL (normal 4.40 to 6.00)

[redacted] **20[redacted] UPPER GI:** NORMAL ESOPHAGUS.HEMATIN IN GASTRIC BODY. BLOOD IN DUODENAL BULB. CHRONIC GASTRITIS. BIOPSIED. ONE OOZING DUODENAL ULCER WITH

VISIBLE VESSEL. INJECTED. CLIPS WERE PLACED.

[redacted] **20[redacted] US VENOUS LOWER EXTREMITY:** NORMAL BILATERAL EXTREMITY VENOUS DOPPLER EXAMINATION. THERE IS NO EVIDENCE OF DEEP VENOUS THROMBOSIS

[redacted] **20[redacted] WBC:** 14.3 X10**3/MCL (normal 4.5 to 11)

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
肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: KNEE INJURY (BOTH KNEES)	19[redacted]
OTHER: BENIGN CYST BLOCKING LEFT KIDNEY	19
OTHER: MEASLES	19
OTHER: CHICKEN POX	19
OTHER: MULTIPLE JOINT PAIN	20
OTHER: ACID REFLUX	20
OTHER: GLAUCOMA	20
OTHER: BACK PAIN	20
OTHER: HEARTBURN	20
OTHER: PLAQUE PSORIASIS	20
OTHER: COAGULATION DEFECT	20
OTHER: PULMONARY EMBOLISM	20
OTHER: PUSTULAR PSORIASIS	20
OTHER: MIXED HYPERLIPIDEMIA	20
OTHER: OSTEOPENIA	20
DEGENERATIVE DISC DISEASE: N/A	20
OTHER: SEASONAL ALLERGIES	20
OTHER: BENIGN NEOPLASM OF COLON	20
OTHER: CHRONIC BRONCHITIS	20
OTHER: NON TOXIC MULTI-NODULAR GOITER	20
OTHER: OSTEOPOROSIS	20
OTHER: RIGHT AND LEFT EYE CATARACT	20
OTHER: DIAPHRAGMATIC HERNIA	20
OTHER: DIVERTICULOSIS OF COLON	20
OTHER: HEMORRHOIDS	20
OTHER: SHORT SEGMENT BARRETTS ESOPHAGUS	20
KIDNEY DISORDER: SURGERY FOR KIDNEY STONES	20
NEPHROLITHIASIS: KIDNEY STONE (LASER SURGERY)	20
HYPERTENSION	20

Prior Procedures	Procedure Year

SURGERY: APPENDECTOMY (APPENDICITIS)	19[redacted]
SURGERY: TOTAL RIGHT KNEE RECONSTRUCTION (FELL FROM THE ROOF)	19[redacted]
SURGERY: BENIGN CYST ON LEFT KIDNEY REMOVAL SURGERY	19[redacted]
SURGERY: PARTIAL HYSTERECTOMY (BENIGN CYST REMOVAL)	19[redacted]
SURGERY: PARTIAL LEFT KIDNEY BYPASS SURGERY (BENIGN CYST ON LEFT KIDNEY)	19[redacted]
SURGERY: TOTAL HYSTERECTOMY (BENIGN CYST REMOVAL)	19[redacted]
SURGERY: LEFT EYE CATARACT SURGERY	20[redacted]
SURGERY: RIGHT EYE CATARACT SURGERY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	15MG	ORAL	QD	[redacted]J[redacted]20[redacted] / 169	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
NAPROXEN	220 mg	PRN	Y-M: 20[redacted]
BIMATOPROST	0.01 %	QD	Y-M: 20[redacted]
BRIMONIDINE	0.2 %	BID	Y-M: 20[redacted]-
INFLIXIMAB	700 mg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted]-
CALCIUM CARBONATE	600/800 OTHER: MG/IU	QD	Y-M: 20[redacted]
INFLIXIMAB	500 mg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted]-
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
CENTRUM SILVER	1 OTHER: TAB	QD	Y-M: 20[redacted]
POLYCARBOPHIL	2 OTHER: GUMMIES	QD	Y-M: 20[redacted]
INFLIXIMAB	100 mg	OTHER: 0 WEEK, 2 WEEK, 6 WEEKS, 0,2,6 THEN EVERY 8 WEEKS	Y-M: 20[redacted]-
USTEKINUMAB	22.5 mg	OTHER: AT 4 WEEKS ,THEN AT 12 WEEKS	Y-M: 20[redacted]-

FOLIC ACID	1 mg	QD	Y-M: 20[redacted]- [redacted] / -49
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]- [redacted] / -19

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
NAPROXEN	220 mg	PRN	Y-M: 20[redacted]	Not reported.
BIMATOPROST	0.01 %	QD	Y-M: 20[redacted]	Not reported.
BRIMONIDINE	0.2 %	BID	Y-M: 20[redacted]- [redacted]	Not reported.
CALCIUM CARBONATE	600/800 OTHER: MG/IU	QD	Y-M: 20[redacted]	Not reported.
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	Not reported.
CENTRUM SILVER	1 OTHER: TAB	QD	Y-M: 20[redacted]	Not reported.
POLYCARBOPHIL	2 OTHER: GUMMIES	QD	Y-M: 20[redacted]	Not reported.
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]- [redacted] / -49	Not reported.
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]- [redacted] / -19	Not reported.
CURCUMA LONGA W/LEVOMEFOLIC ACID/MECOBALAMIN	1/1/500 mg	QD	Y-M: 20[redacted]- [redacted] / 45	Not reported.

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 277
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
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the	NO

Event
SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，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，肺炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は局面型乾癬，肺塞栓症，季節性アレルギー，慢性気管支炎，元喫煙者（1 日 1 箱を 43 年間）及び横隔膜ヘルニアであった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日の朝，被験者は救急サービスに連絡し，息切れを訴えた。被験者は病院に搬送された。被験者は肺炎と診断され，同日入院した。

The patient's past medications include:

REMICADE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

STELARA SOLUTION for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZITHROMYCIN for BRONCHITIS and ACUTE SINUSITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

NASAL SALINE for SINUS CONGESTION ([redacted] 20[redacted] - [redacted] 20[redacted])

TESSALON PERLES for BRONCHITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ZYRTEC for SINUS CONGESTION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.22.0] [10035664]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of PNEUMONIA

- 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
急性腎障害	X			X
菌血症	X			X
硬膜外膿瘍	X			X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PYLONIDAL CYST	19[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: POSTMENOPAUSAL	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CESAREAN SECTION	NOT REPORTED
SURGERY: TUBE LIGATION	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 152	152

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
GOLIMUMAB	50 mg	OTHER: ONCE PER MONTH	Y-M: 20[redacted]
SECUKINUMAB	150 mg	OTHER: ONCE A MONTH	Y-M: 20[redacted] / -243
USTEKINUMAB	45 mg	OTHER: PER MONTH	Y-M: 20[redacted] / -181

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 156	ONGOING
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 156	ONGOING
CLINDAMYCIN	600 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 157
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 157
PIP/TAZO	3.375 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 164
VANCOMYCIN	1000 mg	QID	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 171
CEFAZOLIN	2 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 159	Y-M: 20[redacted] / 189
DOCUSATE	100 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 159	Y-M: 20[redacted] / 189
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 159	Y-M: 20[redacted] / 189

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	ACUTE KIDNEY INJURY AND BACTERIEMIA
Preferred term	急性腎障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 156 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 34): Chloride: 92 [98 - 107] mmol/L; [redacted]20[redacted] (RX DAY 156): Blood Urea Nitrogen: 13.56 [2.5 - 6.43] mmol/L; Creatinine: 181.23 [45.09 - 83.98] umol/L; Glucose: 11.43 [3.89 - 5.5] mmol/L; Hematocrit: 0.28 [0.33 - 0.46] fraction of 1; Hemoglobin: 97 [114 - 154] g/L; Leukocytes: 11 [3.5 - 10] 10^9/L; Platelets: 189 [150 - 450] 10^9/L; Potassium: 3 [3.5 - 5.1] mmol/L; Prothrombin Intl. Normalized Ratio: 1.2 [0.9 - 1.1] RATIO; Sodium: 127 [136 - 146] mmol/L

Microbiology

[redacted]20[redacted] (RX DAY 156): URINE NPTST143-URINE MICROBIOLOGY: POSITIVE-10-50K STAPHYLOCOCCUS AUREUS AND LESS THAN 10K GNR; [redacted]20[redacted] (RX DAY 157): BLOOD NPTST022-BLOOD CULTURE: POSITIVE-GRAM POSITIVE COCCI IN CLUSTERS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 156): CHEST X-RAY: MILD LEFT BASE CONSOLIDATION CONSISTENT WITH INFILTRATE VERSUS ATELECTASIS.; EKG: NORMAL SINUS RHYTHM.

AE Stopped Rx Day	158 (6 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, PERSIST OR SIGNIF DISABILITY/INCAPACITY, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #2: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	ACUTE KIDNEY INJURY AND BACTERIEMIA
Preferred term	菌血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 156 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 34): Chloride: 92 [98 - 107] mmol/L; [redacted]20[redacted] (RX DAY 156): Blood Urea Nitrogen: 13.56 [2.5 - 6.43] mmol/L; Creatinine: 181.23 [45.09 - 83.98] umol/L; Glucose: 11.43 [3.89 - 5.5] mmol/L; Hematocrit: 0.28 [0.33 - 0.46] fraction of 1; Hemoglobin: 97 [114 - 154] g/L; Leukocytes: 11 [3.5 - 10] 10^9/L; Platelets: 189 [150 - 450] 10^9/L; Potassium: 3 [3.5 - 5.1] mmol/L; Prothrombin Intl. Normalized Ratio: 1.2 [0.9 - 1.1] RATIO; Sodium: 127 [136 - 146] mmol/L

Microbiology

[redacted]20[redacted] (RX DAY 156): URINE NPTST143-URINE MICROBIOLOGY: POSITIVE-10-50K STAPHYLOCOCCUS AUREUS AND LESS THAN 10K GNR; [redacted]20[redacted] (RX DAY 157): BLOOD NPTST022-BLOOD CULTURE: POSITIVE-GRAM POSITIVE COCCI IN CLUSTERS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 156): CHEST X-RAY: MILD LEFT BASE CONSOLIDATION CONSISTENT WITH

INFILTRATE VERSUS ATELECTASIS.; EKG: NORMAL SINUS RHYTHM.

AE Stopped Rx Day	158 (6 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, PERSIST OR SIGNIF DISABILITY/INCAPACITY, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #3: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	LOWER BACK EPIDURAL ABSCESS
Preferred term	硬膜外膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 158 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 158): Blood Urea Nitrogen: 8.92 [2.5 - 6.43] mmol/L; Chloride: 109 [98 - 107] mmol/L; Creatinine: 101.66 [45.09 - 83.98] umol/L; Erythrocytes: 2.6 [4 - 5.5] 10^12/L; Glucose: 5.94 [3.89 - 5.5] mmol/L; Hematocrit: 0.26 [0.33 - 0.46] fraction of 1; Hemoglobin: 86 [180 - 140] g/L; Leukocytes: 4 [3.5 - 10] 10^9/L; Lymphocytes: 0.32 [1.16 - 3.18] 10^9/L; Lymphocytes/Leukocytes: 8 [18.2 - 47.4] %; Monocytes: 0.12 [0.29 - 0.71] 10^9/L; Monocytes/Leukocytes: 3 [4.3 - 11] %; NPTST040-CO2: 20 [21 - 32] mmol/L; Neutrophils Band Form/Leukocytes: 12 [0 - 5] %; Neutrophils/Leukocytes: 77 [42.5 - 73.2] %; Potassium: 3.3 [3.5 - 5.1] mmol/L

Microbiology

[redacted]20[redacted] (RX DAY 156): BLOOD NPTST022-BLOOD CULTURE: POSITIVE-STAPHYLOCOCCUS AUREUS; GRAM POSITIVE COCCI IN CLUSTERS.

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 158): LUMBAR SPINE.: EDEMA WITHIN THE L4-5 INTERVERTEBRAL DISC WITH ADJACENT CORTICAL IRREGULARITY AND ENDPLATE CHANGES WHICH IS WORRISOME FOR DISCITIS/OSTEOMYELITIS. VENTRAL EPIDURAL COLLECTION EXTENDING FROM L3 THROUGH; [redacted]20[redacted] (RX DAY 162): BLOOD TRANSFUSION: BLOOD TRANSFUSION; LAMINECTOMY WITH EPIDURAL ABSCESS DRAINAGE: DRAINAGE OF ABSCESS

AE Stopped Rx Day	175 (23 DAYS AFTER LAST TREATMENT)
Duration of AE	18 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	LUMBAR PUNCTURE.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳女性であり，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，急性腎障害，菌血症及び腰部の硬膜外膿瘍の事象を発現した。

Event 1～3 の臨床経過：

関連する病歴は局面型乾癬，乾癬性関節炎，元紙巻タバコ喫煙者（1 日 1 箱を 30 年間）及び少量の現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性腎障害及び菌血症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腰部の硬膜外膿瘍を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性腎障害及び菌血症は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，腰部の硬膜外膿瘍は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，パドルボーディング後に，左手の痛み，発赤・腫脹，幻覚及び腰痛を伴う全身脱力のため入院した。被験者は，転倒して右腕を痛め，ギプスを装着していたが，それ以来，何度も転倒していると報告した。右手に炎症が見られたが，外傷によるものか感染によるものかは不明であった。20[redacted] 年 [redacted] 月 [redacted] 日，尿検査で黄色ブドウ球菌細菌尿が認められた。著しい膿尿は伴っていなかったことから，腎臓への血行性伝播であった。BUN 及びクレアチニンが増加しており，腎不全と一致していた。被験者は菌血症を伴う急性腎障害と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，急性腎障害は軽快し，被験者は 19:14 に退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，左手の痛み／浮腫，薬指の腫脹・発赤，錯乱及び頻回な転倒に加え，発熱及び背部痛のため再入院した。感染，錯乱及び転倒の原因に対する懸念から，脳膿瘍や心内膜炎について調べるために腰椎 MRI を行った。しかし，腰椎 MRI では，骨髄炎，膿瘍，軽度の傍脊椎前部炎症性変化，L4～5 椎間板内浮腫とこれに伴う L3 レベルから S2～3 までの腹側硬膜外腔への貯留物が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，輸血及び硬膜外膿瘍ドレナージのための椎弓切除術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。この被験者の治験参加は完全に中止された。

投与された薬剤は，cleocin，docusate sodium，タイレノール，zofran，vancocin，ゾシン，ancef 及び pepcid であった。

The patient's past medications include:

SIMPONI for PSORIATIC ARTHRITIS ([redacted])

STELARA for PSORIATIC ARTHRITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute kidney injury (10069339) (Acute kidney injury (10069339)) [v.22.0] [10069339]

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

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

Dechallenge: Not Applicable

2) Bacteremia (10003999) (Bacteraemia (10003997)) [v.22.0] [10003999]

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

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

Dechallenge: Not Applicable

3) Epidural abscess (10015010) (Extradural abscess (10061846)) [v.22.0] [10015010]

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 KIDNEY INJURY AND BACTEREMIA

- Investigator: INFECTION

- AbbVie: Events are more likely related to recent fall and left arm injury and are more likely a complication of staphylococcus aureus bacteriuria.

Event of LOWER BACK EPIDURAL ABSCESS

- Investigator: Lumbar puncture.

- AbbVie: Event is more likely a complication of recent fall, left arm injury and bacteremia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BANDS:** 12.0 % (normal 0.0 to 5.0)

[redacted] **20[redacted] BLOOD CULTURE:** Positive - Staphylococcus aureus; Gram positive cocci in clusters.

[redacted] **20[redacted] BLOOD CULTURE:** Gram positive cocci in clusters.

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 38 mg/dL (normal 7 to 18)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 25 mg/dL (normal 7 to 18)

[redacted] **20[redacted] CHEST X-RAY:** Mild left base consolidation consistent with infiltrate versus atelectasis.

[redacted] **20[redacted] CHLORIDE:** 109 MMOL/L (normal 98 to 107)

[redacted] **20[redacted] CO2:** 20 MMOL/L (normal 21 to 32)

[redacted] **20[redacted] CREATININE:** 0.8 mg/dL (normal 0.4 to 1.1)

[redacted] **20[redacted] CREATININE:** 0.8 mg/dL (normal 0.4 to 1.1)

[redacted] **20[redacted] CREATININE:** 1.1 mg/dL (normal 0.4 to 1.1)

[redacted] **20[redacted] CREATININE:** 1.1 mg/dL (normal 0.4 to 1.1)

[redacted] **20[redacted] CREATININE:** 2.05 mg/dL (normal 0.51 to 0.95)

[redacted] **20[redacted] CREATININE:** 2.05 mg/dL (normal 0.51 to 0.95)

[redacted] **20[redacted] CREATININE:** 1.15 mg/dL (normal 0.51 to 0.95)

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

[redacted] **20[redacted] GFR:** 74.7 No unit

[redacted] **20[redacted] GLUCOSE:** 206 mg/dL (normal 70 to 99)

[redacted] **20[redacted] GLUCOSE:** 107 mg/dL (normal 70 to 99)

[redacted] **20[redacted] HEMATOCRIT:** 28.1 % (normal 32.8 to 45.6)

[redacted] **20[redacted] HEMATOCRIT:** 25.5 % (normal >32.8)

[redacted] **20[redacted] HEMOGLOBIN:** 9.7 G/DL (normal 11.4 to 18)

[redacted] **20[redacted] HEMOGLOBIN:** 8.6 G/DL (normal 14 to 18)

[redacted] **20[redacted] INTERNATIONAL NORMALIZED RATIO:** 1.2 Ratio (normal 0.9 to 1.1)

[redacted] **20[redacted] INTERNATIONAL NORMALIZED RATIO:** 1.2 Ratio (normal 0.9 to 1.1)

[redacted] **20[redacted] LYMPHOCYTES:** 8.0 % (normal 18.2 to 47.4)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.32 10^3/uL (normal 1.16 to 3.18)

[redacted] **20[redacted] MONOCYTES:** 3.0 % (normal 4.3 to 11.0)

[redacted] **20[redacted] MONOCYTES ABS:** 0.12 10^3/uL (normal 0.29 to 0.71)

[redacted] **20[redacted] MRI LUMBAR SPINE:** Edema within the L4-5 intervertebral disc with adjacent cortical irregularity and endplate changes which is worrisome for discitis/osteomyelitis. Ventral epidural collection extending from L3 through S2-3 level. This finding is worrisome for epidural phlegmon/abscess.

[redacted] **20[redacted] NEUTROPHILS:** 77.0 % (normal 42.5 to 73.2)

[redacted] **20[redacted] PLATELET COUNT:** 189 10^3/uL (normal 150 to 450)

[redacted] **20[redacted] POTASSIUM:** 3.0 MEQ/L (normal 3.5 to 5.1)

[redacted] **20[redacted] POTASSIUM:** 3.3 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] RED BLOOD CELLS:** 2.58 10^6/uL (normal 4.0 to 5.5)

[redacted] **20[redacted] SERUM BICARBONATE:** 18.1 MEQ/L (normal 17.0 to 30.6)

[redacted] **20[redacted] SERUM BICARBONATE:** 24.3 MEQ/L (normal 17.0 to 30.6)

[redacted] **20[redacted] SERUM BICARBONATE:** 24.3 MEQ/L (normal 17.0 to 30.6)

[redacted] **20[redacted] SODIUM:** 127 MEQ/L (normal 136 to 146)

[redacted] **20[redacted] UREA NITROGEN:** 19 mg/dL (normal 4 to 24)

[redacted] **20[redacted] UREA NITROGEN:** 21 mg/dL (normal 4 to 24)

[redacted] **20[redacted] UREA NITROGEN:** 19 mg/dL (normal 4 to 24)

[redacted] **20[redacted] UREA NITROGEN:** 19 mg/dL (normal 4 to 24)

[redacted] **20[redacted] URINE MICROBIOLOGY:** Positive - 10-50K Staphylococcus aureus and less than 10K GNR

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.0 10^3/uL (normal 3.5 to 10.0)

[redacted] **20**[redacted] **WHITE BLOOD CELLS:** 4.0 10^3/uL (normal 3.5 to 10.0)

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
悪性黒色腫第 3 期	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	7[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: CHICKEN POX	19[redacted]
OTHER: TONCILITIS	19
OTHER: BILATERAL SLIPPED EPIPHYSIS	19
OTHER: SEASONAL ALLERGIES	19
OTHER: PLAQUE PSORIASIS	19
ANEMIA: IRON DEFICIENCY ANEMIA	19
EYE DISEASE/DISORDER: CATARACT BILATERAL EYES	19
OTHER: FRACTURE 2ND LEFT MCP II	19
OSTEOARTHRITIS: BILATERAL KNEES	19
HYPERLIPIDEMIA: HYPERCHOLESTEROLEMIA	19
OTHER: INSOMNIA	19
OSTEOARTHRITIS: BILATERAL HIPS	19
OTHER: MUSCLE SPASM LOWER BACK	20
OTHER: AORTIC REGURGITATION	20
HYPERTENSION	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TONCILECTOMY	19[redacted]
SURGERY: LEFT HIP REPLACEMENT	19
SURGERY: LEFT HIP REPLACEMENT REVISION	19
SURGERY: LEFT KNEE REPLACEMENT	20
SURGERY: RIGHT KNEE REPLACEMENT	20
SURGERY: RIGHT HIP REPLACEMENT	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2 - 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted] / 1	[redacted] / 170	170
ABT-494	15MG	ORAL	QD	[redacted] / 171	[redacted] / 268	98

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CENTRUM	500 OTHER: MCG	QD	Y-M: 19[redacted]
OXYCODONE	75 mg	OTHER: EVERY 8 HOURS	Y-M: 19[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 19[redacted]
CELECOXIB	50 mg	EVERY WEEK	Y-M: 19[redacted]
LEFLUNOMIDE	20 mg	QD	Y-M: 19[redacted]
ATORVASTATIN	40 mg	QD	Y-M: 19[redacted]
FOLIC ACID	1 mg	QD	Y-M: 19[redacted]
ZOLPIDEM	10 mg	QD	Y-M: 19[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 19[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]
METAXALONE	800 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
GOLIMUMAB	50 mg	OTHER: ONCE A MONTH	Y-M: 20[redacted]
GOLIMUMAB	50 mg	OTHER: ONCE A MONTH	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	TID	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
APREMILAST	30 mg	QD	Y-M: 20[redacted]
CERTOLIZUMAB PEGOL	400 mg	OTHER: ONCE A MONTH	Y-M: 20[redacted]
LABETALOL	200 mg	BID	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: ONCE PER MONTH	Y-M: 20[redacted]
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]

HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]
MELOXICAM	15 mg	QD	Y-M: 20[redacted]
USTEKINUMAB	90 mg	OTHER: EVERY 12 WEEKS	Y-M: 20[redacted] / -268

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
CENTRUM	500 OTHER: MCG	QD	Y-M: 19[redacted]	ONGOING
ATORVASTATIN	40 mg	QD	Y-M: 19[redacted]	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 19[redacted]	ONGOING
ZOLPIDEM	10 mg	QD	Y-M: 19[redacted]	ONGOING
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	ONGOING
LABETALOL	200 mg	BID	Y-M: 20[redacted]	ONGOING
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]	ONGOING
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]	ONGOING
MELOXICAM	15 mg	QD	Y-M: 20[redacted]	ONGOING

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

Event Description	SKIN MELANOMA STAGE III LEFT SHOULDER
Preferred term	悪性黒色腫第 3 期
AE Onset Date / Rx Day	[redacted]20[redacted] / 268
Age at AE Onset	7[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 254): OTHER SKIN NPTST125-SHAVE BIOPSY: POSITIVE-MELANOMA

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 254): LEFT UPPER BACK SKIN BIOPSY: MELANOMA PATHELOGIC STAGE AT LEAST T1A

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN ETIOLOGY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の7[redacted]歳男性であり，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，皮膚黒色腫（左肩，第3期）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は局面型乾癬，乾癬性関節炎，非喫煙者及び現飲酒者（1 日 2～4 杯）であった。

被験者は，最初の24週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted]年[redacted]月[redacted]日，ABT-494の盲検投与が開始された。

20[redacted]年[redacted]月[redacted]日，被験者は皮膚黒色腫（左肩，第3期）を発現した。

定期的な皮膚科受診時に皮膚生検が行われた。本事象発現前に徴候や症状はなかった。20[redacted]年[redacted]月[redacted]日，本事象により治験薬の投与が完全に中止された。

Causality for UPADACITINIB (Blinded)

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1) Malignant melanoma stage III (10025670) (Malignant melanoma stage III (10025670)) [v.22.0] [10025670]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of SKIN MELANOMA STAGE III LEFT SHOULDER

- Investigator: Unknown etiology.

- AbbVie: Weak temporal association, with less than 9 months of study drug exposure prior to onset of the event. Advanced age is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] LEFT UPPER BACK SKIN BIOPSY:** Melanoma pathologic, stage at least T1A

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
狭心症	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	6[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
OTHER: BILATERAL SYNDACTLY OF 2ND/3RD TOES	19[redacted]
OTHER: CHICKEN POX	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO LATEX	19
OTHER: UTERINE FIBROIDS	19
ASTHMA	20
EYE DISEASE/DISORDER: DRY EYES	20
EYE DISEASE/DISORDER: ENTROPIAN EYE LIDS	20
CHOLECYSTITIS	20
DRUG ALLERGIES/REACTIONS: ALLERGY TO MORPHINE	20
DRUG ALLERGIES/REACTIONS: ALLERGY TO ULTRAM	20
HYPERTENSION	20
OTHER: HASHIMOTO'S DISEASE	20
OTHER: LEFT SHOULDER PAIN	20
OTHER: PLAQUE PSORIASIS	20
OTHER: MASS ON OVARIES (BENIGN)	20
OTHER: SEASONAL ALLERGIES	20
OTHER: SINUS HEADACHES	20
DIABETES MELLITUS	20
DRUG ALLERGIES/REACTIONS: ALLERGY TO METOPROLOL	20
OTHER: LIPOMAS ON BILATERAL AXILLA, SUPRACLAVICULAR AREA	20
DEPRESSION: DEPRESSION	20
LIVER DISEASE (EXCLUDING HEPATITIS): FATTY LIVER	20
COGNITIVE OR PSYCHIATRIC DISORDER: ANXIETY	20
OTHER: TENSION HEADACHES	20
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE: COPD	20
OTHER: CHEST PALPITATIONS	20
OTHER: PULMONARY NODULES	20
PNEUMONIA	20
OTHER: ALOPECIA	20

Prior Procedures	Procedure Year
SURGERY: PARTIAL HYSTERECTOMY	19[redacted]
SURGERY: CHOLELYCYSECTOMY	20[redacted]
SURGERY: OVARIES EXTRACTED (SECONDARY TO BENIGN MASS)	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 384	215
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 385	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
GLIPIZIDE	10 mg	QD	Y-M: 20[redacted]
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]
USTEKINUMAB	90 mg	OTHER: EVERY 12 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]
METHOTREXATE	0.6 mL	EVERY WEEK	Y-M: 20[redacted]
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]
METHOTREXATE	2.5 mg	QD	Y-M: 20[redacted]
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / -336
INSULIN ASPART	5 OTHER: UNITS	PRN	Y-M: 20[redacted] / -275
INSULIN DETEMIR	15 OTHER: UNITS	QD	Y-M: 20[redacted] / -275

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]	Not reported.
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / -336	Not reported.

GLIPIZIDE	5 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 510
LISINOPRIL	10 mg	QD	Y-M: 20[redacted] / 391	Y-M: 20[redacted] / 443
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted] / 396	Not reported.
AZITHROMYCIN	250 mg	QD	Y-M: 20[redacted] / 408	Y-M: 20[redacted] / 411
GLYCERYL TRINITRATE	.4 mg	PRN	Y-M: 20[redacted] / 441	Not reported.
METOPROLOL	25 mg	BID	Y-M: 20[redacted] / 443	Not reported.
ACICLOVIR	800 mg	QID	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 464
LISINOPRIL	20 mg	QD	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 500

Event #1: Serious Adverse Event

Event Description	ANGINA
Preferred term	狭心症
AE Onset Date / Rx Day	[redacted]20[redacted] / 441
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 441): NPTST027-BN PEPTIDE: 11.9 [0 - 100] pg/mL; NPTST138-TROPONIN-I: 0.03 [0 - 0.05] ng/mL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 441): CHEST X-RAY: NO ACUTE CARDIOPULMONARY ABNORMALITY; ECG: NORMAL SINUS RHYTHM. CANNOT RULE OUT ANTERIOR INFARCT, AGE UNDERTERMINED. ABNORMAL ECG; ECHOCARDIOGRAM: EF=55-60%. GRADE I DIASTOLIC DYSFUNCTION. MILD CONCENTRIC LEFT VENTRICULAR HYPERTROPHY. THE LEFT VENTRICLE IS NORMAL IN SIZE. THERE IS NO THROMBUS. LEFT VENTRICULAR SIZE AND FUNCTION APPEARS NORMAL.; [redacted]20[redacted] (RX DAY 445): NUCLEAR STRESS TEST: EVIDENCE OF SMALL SIZE OF MILD INTENSITY APICAL WALL INFARCT WITHOUT SIGNIFICANT ISCHEMIA.

AE Stopped Rx Day	442
Duration of AE	2 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NEW DEVELOPMENT OF CORONARY ARTERY DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

Generated: [redacted]

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，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，アンギナの事象を発現した。

Event 1 の臨床経過：

関連する病歴は喘息，橋本病，高血圧，局面型乾癬，乾癬性関節炎，糖尿病，不安，胸部の動悸，非喫煙者，非飲酒者及び冠動脈疾患の家族歴であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

冠動脈疾患の家族歴もあった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はアンギナを発現した。20[redacted] 年 [redacted] 月 [redacted] 日，アンギナは消失した。

[redacted] 月 [redacted] 日，被験者は，胸痛，左腕の痛み，嘔吐，発汗及び血圧上昇といった症状により，救急治療室を受診した。被験者は同日入院した。[redacted] 月 [redacted] 日，心電図検査，X 線検査及び心エコー検査が行われた。治療が行われ，アンギナは消失した。[redacted] 月 [redacted] 日，被験者は退院した。外来で核 GXT 検査を行ったところ，軽度の小さな心尖部壁梗塞の徴候が認められたが，著しい虚血は伴っていなかった（日付不明）。治験責任医師は，被験者には高血圧及び 2 型糖尿病の危険因子があると判断した。

投与された薬剤はニトログリセリンであった。

The patient's past medications include:

STELARA for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

HUMIRA for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

OTEZLA for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

LEVEMIR for TYPE II DIABETES (20[redacted] - [redacted] [redacted] 20[redacted])

ULTRAM for UNKNOWN INDICATION

MORPHINE for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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1) Angina pectoris (10002383) (Angina pectoris (10002383)) [v.21.1] [10002383]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of ANGINA

- Investigator: New development of coronary artery disease.

- AbbVie: Risk factors include pre-existing diabetes mellitus, hypertension, and obesity (BMI of 33 at screening)..

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BNP:** 11.9 PG/ML (normal 0.0 to 100.0)

[redacted] **CHEST X-RAY:** No acute cardiopulmonary abnormality

[redacted] **ECHOCARDIOGRAM:** EF=55-60%. Grade I diastolic dysfunction. Mild concentric left ventricular hypertrophy. The left ventricle is normal in size. There is no thrombus. Left ventricular size and function appears normal.

[redacted] **ELECTROCARDIOGRAPHY:** Normal sinus rhythm. Cannot rule out anterior infarct, age undetermined. Abnormal ECG

Unknown date NUCLEAR GXT: Evidence of small size of mild intensity apical wall infarct without significant ischemia.

[redacted] **TROPONIN:** 0.028 NG/ML (normal 0.000 to 0.045)

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
徐脈	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: CHILDHOOD RECURRING TONSILLITIS	19[redacted]
OTHER: OBESITY	19
OSTEOARTHRITIS	19
OTHER: PLAQUE PSORIASIS	19
HEARING DISORDER: SLIGHT HEARING LOSS	20
OTHER: SCROTAL MASS SEROMA	20
OTHER: RIGHT SHOULDER ROTATOR CUFF TEAR	20

Prior Procedures	Procedure Year
SURGERY: ADENOIDECTOMY	19[redacted]
SURGERY: TONSILLECTOMY	19
SURGERY: APPENDECTOMY	19
SURGERY: INGUINAL HERNIA REPAIR	20
SURGERY: SCROTAL MASS ASPIRATION	20
SURGERY: CORRECTIVE SURGERY SECONDARY TO HERNIA REPAIR	20
SURGERY: RIGHT TOTAL SHOULDER REPLACEMENT	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 166	166
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 167	[redacted]20[redacted] / 222	56

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]
PARACETAMOL	600 mg	PRN	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
ABATACEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
VICODIN	5/325 mg	BID	Y-M: 20[redacted]
POTASSIUM	4700 mg	QD	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	ONGOING
PARACETAMOL	600 mg	PRN	Y-M: 20[redacted]	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
VICODIN	5/325 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 39
POTASSIUM	4700 mg	QD	Y-M: 20[redacted]	ONGOING
DEXTROMETHORPHAN HYDROBROMIDE W/DOX	2 OTHER: TABS	OTHER: Q4HRS	Y-M: 20[redacted] / 43	ONGOING

Event #1: Serious Adverse Event

Event Description	SYMPTOMATIC BRADYCARDIA
Preferred term	徐脈
AE Onset Date / Rx Day	[redacted]20[redacted] / 60
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 60): CHEST X-RAY: NORMAL; EKG: SINUS BRADYCARDIA W PREMATURE ATRIAL COMPLEX; [redacted]20[redacted] (RX DAY 61): BILATERAL CAROTID U/S: RIGHT CALCIFIED STENOSIS; CARDIAC STRESS TEST: ASYMPTOMATIC; ECHOCARDIOGRAM: MILD PULMONARY HYPERTENSION; EKG: SINUS BRADYCARDIA W PREMATURE VENTRICULAR COMPLEX

AE Stopped Rx Day	61
Duration of AE	2 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN ETIOLOGY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性であり，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，症候性徐脈の事象を発現した。

Event 1 の臨床経過：

関連する病歴は肥満，乾癬性関節炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は症候性徐脈を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，症候性徐脈は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。診断検査が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

退院時サマリーより：被験者は浮動性めまいにより救急科を受診した。被験者の話では，これまでにこのようなことはなかった。しかし，この数日間は疲労感が増し，3 週間ほど前から胸の詰まりと咳嗽を自覚していた。最初に受診したウォークイン・クリニックでの心電図検査で徐脈性心房細動が認められ，詳細な検査のためそのまま救急科を受診することとなった。

救急科での検査で，頻回な PAC を伴う洞性徐脈が明らかとなった。臨床検査値に特に異常はなく，胸部 X 線検査でも重大な所見は見られなかった。救急科の医師は，被験者が組み入れられた本治験を行っていたリウマチ専門医に連絡した。リウマチ専門医は，徐脈は既知の副作用ではないとした。入院後，テレメトリー及びモニタリングが開始された。前回の心電図検査で徐脈性心房細動が疑われたとの報告があったため，心臓専門医の助言を受けた。入院翌日，心臓負荷検査及び心エコー検査が行われたが，いずれの検査でも重大な所見は認められなかった。被験者の状態は入院期間を通して変わらず，また[redacted]月の心電図検査で頻回な PAC を伴う洞性徐脈が認められたとも報告された。現在の症状は，現在投与中の薬剤の治験とは無関連であると思われた。全体的に，入院中の経過は特に異常なく，悪化や臨床的代償不全も報告されなかった。被験者は医学的に安定していると思われ，退院して，今後はかかりつけ医による経過観察と，外来でのホルター心電図モニタリングのための心臓専門医による経過観察を行うのが妥当と判断された。20[redacted]年[redacted]月[redacted]日，被験者は退院した。

心臓専門医の診察結果より：被験者は症候性徐脈の状態で来院した。被験者は浮動性めまいを訴えたが，最近の疲労増加に伴う心拍数所見は見られなかった。被験者は AV ブロック治療薬を投与されていたわけではなかった。PCP から入手した過去（20[redacted]年）のバイタルサイン測定結果を確認したところ，20[redacted]年[redacted]月の 2 回の測定で心拍数が 51 及び 53 であり，徐脈が認められていた。これは，持病の乾癬性関節炎に対して，新たなリウマチ治療用治験薬の投与が開始される前であった。

被験者は病的肥満であり，早発性 CAD の家族歴を有していた。被験者には睡眠時無呼吸の一因が存在したと考えられた。実際，被験者は夜間にいびきをかいている。

Causality for ABT-494 (Blinded)

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1) Bradycardia (10006093) (Bradycardia (10006093)) [v.21.0] [10006093]

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 ABT-494 (Blinded)

Event of SYMPTOMATIC BRADYCARDIA

- Investigator: Unknown etiology.

- AbbVie: Event is more likely related to abnormal EKG at screening. Additionally bradycardia was noted on two occasions in [redacted] 20[redacted] and appears to be pre-existing.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BILATERAL CAROTID ULTRASOUNDS:** right calcified stenosis Interpretation Summary: The right common carotid artery shows no evidence of disease. The right external carotid artery shows evidence of <50% disease. The right bulb/internal carotid artery shows evidence of 20-39% calcified stenosis. Spectral Doppler flow evaluation of the innominate artery shows no evidence of a hemodynamically significant stenosis. Spectral Doppler flow evaluation of the right proximal subclavian artery shows no evidence of a hemodynamically significant stenosis. The right vertebral artery demonstrates antegrade flow. The left common carotid artery shows no evidence of disease. The left external carotid artery shows evidence of <50% disease. The left bulb/proximal internal carotid artery shows evidence of a 1-19%stenosis with homogeneous plaque. Spectral Doppler flow evaluation of the left proximal subclavian artery show no evidence of a hemodynamically significant stenosis. The left vertebral artery demonstrates antegrade flow.

[redacted] **20[redacted] BLOOD PRESSURE:** 157/88

Unknown date CALCIUM: 9.2 mg/dL

[redacted] **20[redacted] CARDIAC STRESS TEST:** asymptomatic In conclusion, low risk EKG portion of exercise nuclear stress test with the patient showing chronotropic competency.No evidence of ischemia Diaphragmatic attenuation. Normal left ventricular systolic function No evidence for transient ischemic dilatation.

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

[redacted] **20[redacted] CK MB FRACTION:** 3.10 NG/ML

[redacted] **20[redacted] ECHOCARDIOGRAM:** Interpretation Summary: The left ventricular ejection fraction is estimated at 60%. There is mild concentric left ventricular hypertrophy. The right ventricle demonstrates normal systolic function. The left atrium is normal in size. The estimated peak right ventricular systolic pressure is 41 mmHg, consistent with mild pulmonary hypertension. There is no evidence of a pericardial effusion.

[redacted] **20[redacted] EKG:** sinus bradycardia w premature atrial complex

[redacted] **20**[redacted] **EKG:** sinus bradycardia w premature ventricular complex

[redacted] **20**[redacted] **ELECTROCARDIOGRAM:** Screening ECG: atrial fibrillation;

[redacted] **20**[redacted] **GLUCOSE:** 84 mg/dL

[redacted] **20**[redacted] **HCT:** 42.7 %

[redacted] **20**[redacted] **HEART RATE:** 48 No units

[redacted] **20**[redacted] **HGB:** 14.4 G/DL

[redacted] **20**[redacted] **ISTAT TROPONIN:** 0.03 NG/ML

[redacted] **20**[redacted] **ISTAT TROPONIN:** 0.03 NG/ML

[redacted] **20**[redacted] **PLATELET COUNT:** 320 K/uL

[redacted] **20**[redacted] **POTASSIUM:** 4.6 MMOL/L

[redacted] **20**[redacted] **PULSE OXIMITER:** 95 No units

[redacted] **20**[redacted] **RESPIRATORY RATE:** 20 No units

[redacted] **20**[redacted] **TROPONIN:** 0.08 NG/ML

[redacted] **20**[redacted] **WBC:** 10.2 K/uL

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
子宮平滑筋腫	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 15 mg QD	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PREMENSTRUAL SYNDROME	20[redacted]
OTHER: UTERINE FIBROIDS	20
GASTROESOPHAGEAL REFLUX DISEASE	20
HYPERLIPIDEMIA	20
OTHER: ELEVATED C-REACTIVE PROTEIN BLOOD LEVEL	20
OTHER: PLAQUE PSORIASIS	20
DRUG ALLERGIES/REACTIONS: REMICADE - DRUG ALLERGY	20
DEPRESSION: MAJOR	20
OTHER: HAIR LOSS	20
OTHER: ABNORMAL LYMPHOCYTE RESULT	20
OTHER: ABNORMAL MONOCYTE RESULT	20
OTHER: ABNORMAL WHITE BLODD CELL COUNT	20

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted] / 1	[redacted] / 174	174
ABT-494	15MG	ORAL	QD	[redacted] / 175	[redacted] / 392	218
ABT-494	15MG	ORAL	QD	[redacted] / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BIOTIN	1000 ug	QD	Y-M: [redacted]
CURCUMA LONGA	500 mg	QD	Y-M: [redacted]
DICLOFENAC	35 mg	QD	Y-M: [redacted]
ESOMEPRAZOLE	40 mg	QD	Y-M: [redacted]
PRAVASTATIN	20 mg	QD	Y-M: [redacted]
VICODIN	10 325 mg	PRN	Y-M: [redacted]
APREMILAST	30 mg	BID	Y-M: [redacted]
SECUKINUMAB	150 mg	OTHER: ONCE A MONTH	Y-M: [redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BIOTIN	1000 ug	QD	Y-M: [redacted]	Not reported.
CURCUMA LONGA	500 mg	QD	Y-M: [redacted]	Not reported.
DICLOFENAC	35 mg	QD	Y-M: [redacted]	Not reported.
ESOMEPRAZOLE	40 mg	QD	Y-M: [redacted]	Not reported.
PRAVASTATIN	20 mg	QD	Y-M: [redacted]	Not reported.
VICODIN	10 325 mg	PRN	Y-M: [redacted]	Not reported.
ESCITALOPRAM	20 mg	QD	Y-M: [redacted] / 84	Not reported.

Event #1: Serious Adverse Event

Event Description	UTERINE FIBROIDS
Preferred term	子宮平滑筋腫
AE Onset Date / Rx Day	[redacted]20[redacted] / 127
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 142): Hemoglobin: 134 [120 - 140] g/L; Leukocytes: 15 [4.8 - 10.8] 10^9/L; NPTST114-PT/INR: 0.9 [0.9 - 1.1] sec; Platelets: 561 [130 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 146): Hemoglobin: 125 [120 - 140] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 145): ROBOTIC LAPROSCOPIC HYSTERECTOMY WITH BILATERAL SALPINGECTOMY AND CYSTOSCOPY: SUCCESSFUL

AE Stopped Rx Day	145
Duration of AE	19 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HISTORY OF UTERINE FIBROIDS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳女性であり，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，子宮類線維症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は月経前症候群，子宮類線維症及び乾癬性関節炎であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は子宮類線維症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，子宮類線維症は消失した。

被験者は，10 ヵ月に及ぶ不規則な月経周期，重度の大量凝血塊及び組織排出の訴えにより，産婦人科医を受診した。子宮摘出術が予定された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，ロボット支援腹腔鏡下子宮摘出術，両側卵管摘除術及び膀胱鏡検査が行われた。手術は成功し，合併症は見られなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

REMICADE for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Uterine fibroids (10046784) (Uterine leiomyoma (10046798)) [v.22.0] [10046784]

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 UTERINE FIBROIDS

- Investigator: History of uterine fibroids.

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF UTERINE FIBROIDS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] HEMOGLOBIN:** 13.4 G/DL (normal 12.0 to 14.0)

[redacted] **20[redacted] HEMOGLOBIN:** 12.5 G/DL (normal 12.0 to 14.0)

[redacted] **20[redacted] INR:** 0.9 No Unit

[redacted] **20[redacted] PLATELET COUNT:** 561 X10**3/MCL (normal 130 to 400)

[redacted] **20[redacted] WBC:** 14.99 X10**3/MCL (normal 4.8 to 10.8)

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
失見当識	X			
浮動性めまい	X			
転倒	X			
会話障害	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: NEPHROLITHIASIS HISTORY	NOT REPORTED
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: DEEP VEIN THROMBOSIS	20[redacted]
DEPRESSION: NO SUICIDAL IDEATION NO EVENTS	20[redacted]
BENIGN PROSTATIC HYPERPLASIA	20[redacted]
HYPERTENSION	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TRANSURETHRAL RESECTION OF THE PROSTATE	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 88	88

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CLOBETASOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
QUETIAPINE	200 mg	QD	Y-M: 20[redacted]
ETANERCEPT	UNK mg	EVERY WEEK	Y-M: 20[redacted]-
METHOTREXATE	UNK mg	EVERY WEEK	Y-M: 20[redacted]-
IBUPROFEN	200 mg	OTHER: 3 TIME A WEEK	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
QUETIAPINE	200 mg	QD	Y-M: 20[redacted]	ONGOING
IBUPROFEN	200 mg	OTHER: 3 TIME A WEEK	Y-M: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL
Preferred term	失見当識
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DATA IS UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL
Preferred term	浮動性めまい
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DATA IS UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL
Preferred term	転倒
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DATA IS UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #4: Serious Adverse Event

Event Description	DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL
Preferred term	会話障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
NOT REPORTED

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DATA IS UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者はプエルトリコの 6[redacted] 歳男性であり，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，浮動性めまい，発語困難，見当識障害及び転倒の事象を発現した。

Event 1～4 の臨床経過：

関連する病歴は深部静脈血栓症，うつ病，乾癬性関節炎，高血圧，非喫煙者及び非飲酒者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は浮動性めまい，発語困難，見当識障害及び転倒を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は転倒のため入院した。発語困難，失見当識及び浮動性めまいが認められた。被験者が追跡不能となったため，これ以上の情報の入手は不可能である。

Causality for ABT-494 (Blinded)

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1) Speech disorder (10041466) (Speech disorder (10041466)) [v.22.0] [10041466]

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

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

Dechallenge: No

2) Fall (10016173) (Fall (10016173)) [v.22.0] [10016173]

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

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

Dechallenge: No

3) Disorientated (10013394) (Disorientation (10013395)) [v.22.0] [10013394]

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

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

Dechallenge: No

4) Dizziness (10013573) (Dizziness (10013573)) [v.22.0] [10013573]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL

- Investigator: Data is unknown

- AbbVie: Risk factors include age, hypertension, and history of deep vein thrombosis.

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
中咽頭扁平上皮癌	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: DYSFUNCTIONAL UTERINE BLEEDING	20[redacted]
DRUG ALLERGIES/REACTIONS: NAPROSYN	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 166	166
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 167	[redacted]20[redacted] / 330	164

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETANERCEPT	UNK mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	UNK mg	EVERY WEEK	Y-M: 20[redacted]
OVIDON	0.3 mg	QD	Y-M: 20[redacted] / -291
FOLIC ACID	2 mg	QD	Y-M: 20[redacted] / -261
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -261

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	2 mg	QD	Y-M: 20[redacted] / -261	ONGOING
FAMOTIDINE	UNKNOWN mg	OTHER: ONCE	Y-M: 20[redacted] / 56	ONGOING
CILEST	250 mg	QD	Y-M: 20[redacted] / 62	ONGOING
COLECALCIFEROL	20,000 IU	EVERY WEEK	Y-M: 20[redacted] / 167	ONGOING
THROAT PREPARATIONS	1 OTHER: SPRAY	BID	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 330
CEFALEXIN	500 mg	BID	Y-M: 20[redacted] / 330	ONGOING
PARACETAMOL	500 mg	BID	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 337
CEFAZOLIN	1 g	TID	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
KETOROLAC	15 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
KETOROLAC	30 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
PARACETAMOL	325 mg	QID	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408

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

Event Description	RIGHT SIDE TONGUE SQUAMOUS CELL CARCINOMA, MODERATELY DIFFERENTIATED, INVASIVE IN SITU HYBRIDIZATION OF HPV IN PROGRESS.
Preferred term	中咽頭扁平上皮癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 323
Age at AE Onset	2[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 330): BIOPSY TONGUE RIGHT LATERAL: SQUAMOUS CELL CARCINOMA, MODERATELY DIFFERENTIATED, INVASIVE. IN SITU HYBRIDIZATION OF HPV IN PROGRESS, A REPORT WILL FOLLOW; [redacted]20[redacted] (RX DAY 346): PET/CT SCAN: 1. HYPERMATABOLIC DENSITY IN THE RIGHT SIDE OF THE TONGUE AS DESCRIBED ABOVE CONSISTENT WITH HEAD AND NECK CT SCAN WITH F-18 FDG AVID ACTIVE NEOPLSTIC PROCESS. CORRELATION WITH HEAD AND NECK CT SCAN W; [redacted]20[redacted] (RX DAY 365): CERVICAL/VAGINAL-THIN-PREP: NEGATIVE FOR INTRAEPITHELIAL; HPV GENOTYPE 18/45: NEGATIVE; HPV GENPTYPE 16: POSITIVE; HUMAN PAPILLOMA VIRUS- OTHER HIGH RISK TYPES: POSITIVE; [redacted]20[redacted] (RX DAY 385): EKG: T WAVE INVERSION NON SPECIFIC - NOT CLINICALLY SIGNIFICANT; [redacted]20[redacted] (RX DAY 392): TRACHEOSTOMY TUBE AND GASTRONOMY TUBE PLACEMENT: SUBJECT WAS DISCHARGED AFTER PROCEDURES

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INVASIVE IN SITU HYBRIDIZATION OF HPV IN PROGRESS.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者はプエルトリコの 2[redacted] 歳女性であり，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，右側舌扁平上皮癌（中分化型，浸潤性，HPV の in situ ハイブリダイゼーション実施中）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は局面型乾癬，乾癬性関節炎，非喫煙者及び少量の現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右側舌扁平上皮癌（中分化型，浸潤性，HPV の in situ ハイブリダイゼーション実施中）を発現した。

被験者は，右側舌の潰瘍のため，規定外来院した。被験者は，疼痛，腫脹及び痛みを伴う嚥下困難を発現した。治験責任医師は患部の生検を依頼した。20[redacted] 年 [redacted] 月 [redacted] 日，右側舌の生検が行われた。結果は，扁平上皮癌（中分化型，浸潤性）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は治療のため入院した。被験者は意識清明・見当識正常で協力的であった。被験者の予後は不良であった。同日，気管切開チューブ及び胃瘻造設術チューブの留置が行われた。放射線療法のための評価が進行中であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，sore throat spray，アセトアミノフェン及び cephalexin であった。

The patient's past medications include:

ENBREL for PSORIATIC THRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METROTEXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

NAPROSYN for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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1) HPV positive oropharyngeal squamous cell carcinoma (10081287) (Oropharyngeal squamous cell carcinoma (10031112)) [v.21.1] [10081287]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of RIGHT SIDE TONGUE SQUAMOUS CELL CARCINOMA, MODERATELY DIFFERENTIATED, INVASIVE IN SITU HYBRIDIZATION OF HPV IN PROGRESS

- Investigator: Invasive in situ hybridization of HPV in progress.

- AbbVie: Risk factor includes HPV infection per PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] HUMAN PAPILLOMA: positive

[redacted] 20[redacted] BIOPSY TONGUE RIGHT LATERAL: Squamous cell carcinoma, moderately differentiated, invasive. In situ hybridization of HPV in progress, report will follow.

[redacted] 20[redacted] CERVICAL /VAGINAL THIN PREP: NEGATIVE FOR INTRAEPITHELIAL

[redacted] 20[redacted] EKG: T wave inversion non specific- not clinically significant

[redacted] 20[redacted] HPV GENOTYPE 16: positive

[redacted] 20[redacted] HPV GENOTYPE 18/45: negative

[redacted] 20[redacted] PET/CT SCAN: HYPERMATABOLIC DENSITY IN THE RIGHT SIDE OF THE TONGUE AS DESCRIBED ABOVE CONSISTENT WITH HEAD AND NECK CT SCAN WITH F-18 FDG AVID ACTIVE NEOPLSTIC PROCESS. CORRELATION WITH HEAD AND NECK CT SCAN WITH IV CONTRAST IS RECOMENDED. 2. SYMMETRIC INTENSE F-18 FDG UPTAKE IN THE WALDEYERS RING IS NOTED. ALTHOUGHT IT COULD BE REACTIVE, PLEASE CORRELATE CLINICALLY TO EXCLUDE OTHER PATHOLOGY. 3. NO HYPERBOLIC FOCI TO SUGGEST F-18 FDG AVIS DISTANT METASTATIC DISEASE AT THE PRESENT TIME.

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
腹痛	X	X		
下痢	X	X		

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: FIBROCYSTIC BREAST DISEASE	20[redacted]
DRUG ALLERGIES/REACTIONS: SULFA ALLERGY; HIVES WITH THROAT CLOSURE	20[redacted]
OTHER: DEVIATED SEPTUM	20[redacted]
OTHER: ANXIETY	20[redacted]
ANEMIA: DUE TO UTERINE FIBROIDS	20[redacted]
OTHER: LOW BACK PAIN (DEGENERATIVE DISC DISEASE LUMBAR SPINE)	20[redacted]
OTHER: UTERINE FIBROIDS	20[redacted]
OTHER: BENIGN CYST ON LIVER	20[redacted]
OTHER: OCCASIONAL ORAL ULCERS	20[redacted]
OTHER: ENVIRONMENTAL ALLERGIES	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: OCCASIONAL	20[redacted]
OTHER: CHRONIC GASTRITIS	20[redacted]
OTHER: DIVERTICULOSIS	20[redacted]
OTHER: EXTERNAL HEMORRHOIDS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: BENIGN BREAST CYST REMOVAL	20[redacted]
SURGERY: REPAIR DEVIATED SEPTUM	20[redacted]
SURGERY: HYSTERECTOMY (DUE TO FIBROIDS)	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 147	147

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
VENLAFAXINE	37.5 mg	QD	Y-M: 20[redacted]
FAMOTIDINE	20 mg	PRN	Y-M: 20[redacted]
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted]-
SECUKINUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]-
ASCORBIC ACID	1000 mg	QD	Y-M: 20[redacted]-
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]-
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted]
IBUPROFEN	600 mg	QD	Y-M: 20[redacted]-[redacted] / -308
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted] / -62

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
VENLAFAXINE	37.5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 330
FAMOTIDINE	20 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 167
ASCORBIC ACID	1000 mg	QD	Y-M: 20[redacted]	Not reported.
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	Not reported.
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted]	Not reported.
IBUPROFEN	600 mg	QD	Y-M: 20[redacted] / 308	Y-M: 20[redacted] / 163
HYDROXYCHLOROQUINE	200 mg	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 158
CIPROFLOXACIN	250 mg	BID	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
NITROFURANTOIN	100 mg	BID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 155
DIPHENHYDRAMINE	37.5 mg	PRN	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 187
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 153	Y-M: 20[redacted] / 155
PHENAZOPYRIDINE	100 mg	TID	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 156
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 158	Y-M: 20[redacted] / 167
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 159	Y-M: 20[redacted] / 162
NYSTATIN	400,000 OTHER: UNIT	QID	Y-M: 20[redacted] / 160	Y-M: 20[redacted] / 169
DICYCLOVERINE	20 mg	QD	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 163
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 178
HYOSCYAMINE	0.125 mg	QID	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 184
MAALOX	1 OTHER: TABLESPOON	BID	Y-M: 20[redacted] / 168	Not reported.
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 168	Not reported.
BIFIDOBACTERIUM INFANTIS	4 mg	QD	Y-M: 20[redacted] / 176	Not reported.

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

Event Description	LEFT SIDE ABDOMINAL PAIN RADIATING TO LEFT FLANK UNKNOWN ETIOLOGY, DIARRHEA

Preferred term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 156 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 162): Glucose: 5.77 [3.89 - 5.5] mmol/L; Leukocytes: 8.1 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 9.6 [24 - 44] %; Neutrophils/Leukocytes: 81.3 [45 - 75] %; [redacted]20[redacted] (RX DAY 163): Calcium: 2.1 [2.12 - 2.52] mmol/L; Protein: 62 [64 - 82] g/L; [redacted]20[redacted] (RX DAY 164): Albumin: 33 [34 - 50] g/L; Calcium: 2.02 [2.12 - 2.52] mmol/L; Protein: 59 [64 - 82] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 157): CT SCAN OF ABDOMEN/PELVIS WITH CONTRAST: UNREMARKABLE; [redacted]20[redacted] (RX DAY 162): CHEST X-RAY: NORMAL; [redacted]20[redacted] (RX DAY 164): ENDOSCOPY: NORMAL EXCEPT FOR GASTRITIS AS IN MEDICAL HISTORY

AE Stopped Rx Day	184 (37 DAYS AFTER LAST TREATMENT)
Duration of AE	29 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	LEFT SIDE ABDOMINAL PAIN RADIATING TO LEFT FLANK UNKNOWN ETIOLOGY, DIARRHEA
Preferred term	下痢
AE Onset Date / Rx Day	[redacted]20[redacted] / 156 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 162): Glucose: 5.77 [3.89 - 5.5] mmol/L; Leukocytes: 8.1 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 9.6 [24 - 44] %; Neutrophils/Leukocytes: 81.3 [45 - 75] %; [redacted]20[redacted] (RX DAY 163): Calcium: 2.1 [2.12 - 2.52] mmol/L; Protein: 62 [64 - 82] g/L; [redacted]20[redacted] (RX DAY 164): Albumin: 33 [34 - 50] g/L; Calcium: 2.02 [2.12 - 2.52] mmol/L; Protein: 59 [64 - 82] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 157): CT SCAN OF ABDOMEN/PELVIS WITH CONTRAST: UNREMARKABLE; [redacted]20[redacted] (RX DAY 162): CHEST X-RAY: NORMAL; [redacted]20[redacted] (RX DAY 164): ENDOSCOPY: NORMAL EXCEPT FOR GASTRITIS AS IN MEDICAL HISTORY

AE Stopped Rx Day	184 (37 DAYS AFTER LAST TREATMENT)
Duration of AE	29 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳女性であり，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，左側腹部に放散する原因不明の左腹部痛及び下痢の事象を発現した。

Event 2 及び 3 の臨床経過：

関連する病歴は局面型乾癬，良性肝嚢胞，乾癬性関節炎，慢性胃炎，胃食道逆流性疾患，元喫煙者（1 日 0.5 箱を 5 年間），憩室症及び元飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左側腹部に放散する原因不明の左腹部痛及び下痢を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左側腹部に放散する原因不明の左腹部痛及び下痢は消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は尿路感染（非重篤）を発現した。UTI により治験薬の投与が中止された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はシプロフロキサシンに対するアレルギー反応（非重篤）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日にはピリジウム不耐性（非重篤）も認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腹痛のため救急治療室（ER）を受診し，腹部／骨盤部の造影 CT スキャン検査及び臨床検査を受けた。検査結果はすべて異常なしであった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，痙攣性の鋭い痛みを伴って左側腹部に放散する間欠性で中等度の左腹部痛と，これに伴う下痢を訴えて，ER を受診した。被験者によると，発熱，悪寒，嘔吐，排尿困難，血便，食欲の変化及び体重減少はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，清澄流動食が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，内視鏡検査が行われたが，結果は胃炎が認められた以外は異常なしであった。腹痛の原因は不明であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，マーロックス，pantoprazole，align probiotic，hyoscyamine，zofran 及び bentyl であった。

The patient's past medications include:

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SECUKINUMAB for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENBREL for PSORIATIC ARTHRITIS ([redacted])

CIPROFLOXACIN for URINARY TRACT INFECTION ([redacted])

MACROBID for URINARY TRACT INFECTION ([redacted])

PREDNISONE for ALLERGIC REACTION CIPROFLOXACIN ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Abdominal pain localized (10062367) (Abdominal pain (10000081)) [v.22.0] [10062367]

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

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

Dechallenge: Not Applicable

2) Diarrhea (10012727) (Diarrhoea (10012735)) [v.22.0] [10012727]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of LEFT SIDE ABDOMINAL PAIN RADIATING TO LEFT FLANK UNKNOWN ETIOLOGY, DIARRHEA

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing chronic gastritis and diverticulosis, as well as recent urinary tract infection.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] 20[redacted] **CALCIUM:** 8.4 mg/dL (normal 8.5 to 10.1)

[redacted] 20[redacted] **CALCIUM:** 8.1 mg/dL (normal 8.5 to 10.1)

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

[redacted] 20[redacted] **CT SCAN OF ABDOMEN AND PELVIS WITH CONTRAST:** Unremarkable

[redacted] 20[redacted] **ENDOSCOPY:** Normal except for gastritis as in medical history

[redacted] 20[redacted] **GLUCOSE:** 104 mg/dL (normal 70 to 99)

[redacted] 20[redacted] **LYMPHOCYTES:** 9.6 % (normal 24 to 44)

[redacted] 20[redacted] **NEUTROPHILS:** 81.3 % (normal 45 to 78)

[redacted] 20[redacted] **TOTAL PROTEIN:** 6.2 G/DL (normal 6.4 to 8.2)

[redacted] 20[redacted] **TOTAL PROTEIN:** 5.9 G/DL (normal 6.4 to 8.2)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 8.1 TH/UL (normal 4.5 to 11)