## M15-572 試験（投与 56 週時）

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| 治験の標題：<br>1 種類以上の非生物学的疾患修飾性抗リウマチ薬（DMARD）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）とプラセボ及びアダリムマブとの第 III 相ランダム化二重盲検比較試験-*SELECT-PsA1* | |
| 治験実施施設：<br>44 ヵ国（アルゼンチン，オーストラリア，ベラルーシ，ベルギー，ボスニア・ヘルツェゴビナ，ブラジル，ブルガリア，カナダ，チリ，中国，香港，コロンビア，クロアチア，チェコ共和国，エストニア，ドイツ，ギリシャ，ハンガリー，アイルランド，イスラエル，イタリア，日本，韓国，ラトビア，リトアニア，マレーシア，メキシコ，オランダ，ニュージーランド，ポーランド，ポルトガル，ロシア連邦，セルビア，シンガポール，スロバキア，スロベニア，南アフリカ，スペイン，スイス，台湾，トルコ，イギリス，ウクライナ，米国［プエルトリコを含む］），281 施設 | |
| 治験責任医師：<br>[redacted] FRCP, PhD，他 | |
| 公表文献（参考資料）：<br>1 報 | |
| 治験期間（年数）：<br>最初の被験者の初回来院日：2017 年 4 月 27 日<br>最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日（投与 56 週時） | 開発のフェーズ：III |

目的：

第 1 ピリオド

主要目的：

1 種類以上の非生物学的疾患修飾性抗リウマチ薬（以下「non-bDMARD」）投与で効果不十分又は忍容性のない（以下「non-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（乾癬性関節炎の症状・徴候）をプラセボ又はアダリムマブと比較する。

副次目的：

（1）non-bDMARD-IR（1 種類以上）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）を投与したときの有効性（構造的損傷の防止）をプラセボと比較する。
（2）non-bDMARD-IR（1 種類以上）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又はアダリムマブと比較する。

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。

56 週間治験総括報告書（以下「CSR W56」）のデータカットオフ日（20[redacted] 年 [redacted] 月 [redacted] 日）時点において，第 1 ピリオドは完了していた（すなわち，全被験者が完了又は中止していた）。第 2 ピリオドは実施中である。本項には，第 1 ピリオドの投与 56 週時までの有効性データ及び CSR W56 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：1640 名，解析時：1705 名（ウパダシチニブ 15 mg 群：430 名，ウパダシチニブ 30 mg 群：423 名，アダリムマブ群：429 名，プラセボ→ウパダシチニブ 15 mg 群：211 名，プラセボ→ウパダシチニブ 30 mg 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本試験に組み入れた。

以下のすべ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［以下「TJC」］が 3 ヵ所以上［68 関節に基づく］及び腫脹関節数［以下「SJC」］が 3 ヵ所以上［66 関節に基づく］と定義）
- スクリーニング時に中央画像判定機関による X 線画像の判定で 1 ヵ所以上の骨びらんを有する，又は高感度 C-反応性蛋白（以下「hsCRP」）が施設基準値上限を上回る場合のいずれかに該当する
- 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 non-bDMARD によるこれまでの治療で効果不十分（最低 12 週間の治療で効果が認められない）である，又は疾患修飾性抗リウマチ薬（以下「DMARD」）に忍容性がない若しくは DMARD が禁忌であると治験責任医師に判定されている

以下の患者を除外した：

- 生物学的免疫調整剤，ヤヌスキナーゼ阻害薬による治療歴がある
- 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
- ベースライン時に 3 種類以上の 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 non-bDMARD 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
- 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（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は，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組入れ可能とした）
- 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，科学的及び規則上の目的を達成するために，全世界の約 350 施設で約 1640 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，プラセボ及び実薬対照投与期間，並びにその後の追加 32 週間の実薬対照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 5 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，及び 5）70 日間の電話連絡による追跡調査期間。

適格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，指趾炎の有無，腱付着部炎の有無によって層別化（ただし，中国人及び日本人の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，2:2:2:1:1 の割合で以下の 5 つの投与群のうち 1 つにランダム化する計画とした。

グループ 1：ウパダシチニブ 15 mg 1 日 1 回（N = 410）
グループ 2：ウパダシチニブ 30 mg 1 日 1 回（N = 410）
グループ 3：アダリムマブ 40 mg 隔週（N = 410）
グループ 4：プラセボ→ウパダシチニブ 15 mg 1 日 1 回（N = 205）
グループ 5：プラセボ→ウパダシチニブ 30 mg 1 日 1 回（N = 205）
ヒドロキシクロロキン，スルファサラジン，ブシラミン又はイグラチモドを併用投与していた被験者は約 15%を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 5 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]
アダリムマブ 40 mg，1 mL プレフィルドシリンジ剤（皮下），バルクロット番号：[redacted]4
アダリムマブに対応するプラセボの 1 mL プレフィルドシリンジ剤（皮下），バルクロット番号：[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 24 週時の乾癬性関節炎用改変 Sharp/van der Heijde スコア（以下「SHS」）の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 24 週時の腱付着部炎が消失した被験者（リーズ腱付着部炎指標［以下「LEI」］= 0）の割合
- 投与 12 週時の ACR20 反応率（アダリムマブに対するウパダシチニブの非劣性）
- 投与 12 週時における Short Form 36 項目健康調査票（以下「SF-36」）の身体的健康度（以下「PCS」）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 12 週時の ACR20 反応率（アダリムマブに対するウパダシチニブの優越性）
- 投与 24 週時の指趾炎が消失した被験者（リーズ指趾炎指標［以下「LDI」］= 0）の割合
- 投与 12 週時の患者による疼痛度評価（数値化格付けスケール［以下「NRS」］）のベースラインからの変化量（アダリムマブに対するウパダシチニブの優越性）
- 投与 12 週時の HAQ-DI のベースラインからの変化量（アダリムマブに対するウパダシチニブの優越性）

- 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（ウパダシチニブの各用量とプラセボの比較）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（以下「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：

- X 線画像上で疾患進行が認められない被験者（SHS のベースラインからの変化量が 0 以下及び 0.5 以下と定義）の割合
- 関節裂隙狭小化スコア及び関節びらんスコアのベースラインからの変化量
- ACR 反応率の個々の項目におけるベースラインからの変化量（TJC のベースラインからの変化量［0～68］，SJC のベースラインからの変化量［0～66］，疾患活動性 NRS の医師による全般的評価［PGA］のベースラインからの変化量，疾患活動性 NRS の患者による全般的評価［PtGA］のベースラインからの変化量，疼痛 NRS の患者による評価のベースラインからの変化量，HAQ-DI のベースラインからの変化量，hsCRP のベースラインからの変化量）
- ACR20 / 50 / 70 反応率
- MDA を達成した被験者の割合
- LDI のベースラインからの変化量（ベースラインの LDI が 0 を超えていた被験者が対象）
- 指趾炎数のベースラインからの変化量（ベースラインの LDI が 0 を超えていた被験者が対象）
- 指趾炎が消失した被験者の割合（ベースラインの LDI が 0 を超えていた被験者が対象）
- LEI のベースラインからの変化量（ベースラインの LEI が 0 を超えていた被験者が対象）
- 腱付着部炎が消失した被験者（LEI =0）の割合（ベースラインの LEI が 0 を超えていた被験者が対象）
- 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（ベースラインの SPARCC 腱付着部炎指標が 0 を超えていた被験者が対象）
- 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（ベースラインの SPARCC 腱付着部炎指標が 0 を超えていた被験者が対象）
- 腱付着部炎総数のベースラインからの変化量（ベースラインの腱付着部炎総数が 0 を超えていた被験者が対象）
- 腱付着部炎が消失した被験者（腱付着部炎総数= 0）の割合（ベースラインの腱付着部炎総数が 0 を超えていた被験者が対象）
- PASI75 / 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）
- 乾癬の sIGA スコアの 0 又は 1 を達成した被験者の割合（ベースラインの sIGA が 2 以上の被験者が対象）
- 体表面積-乾癬（以下「BSA-Ps」）のベースラインからの変化量（ベースラインで BSA-Ps が 0 を超えていた被験者が対象）
- 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）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 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
- SAPS 質問票におけるベースラインからの変化量
- バース強直性脊椎炎疾患活動性指標（以下「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）
- 朝のこわばり（BASDAI 質問票 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（BASDAI 質問票 5，0～10）のベースラインからの変化量
- 朝のこわばりの期間（BASDAI 質問票 6，0～10）のベースラインからの変化量
- 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）
- 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

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，バイタイルサイン，身体検査，臨床検査（血液学的検査，血液生化学検査及び尿検査）及び製品の品質に関する苦情・不具合

統計手法：

有効性：

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。

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。X 線画像データ以外の 2 値変数の解析には，as observed（以下「AO」）データ及び欠測値を補完した AO データを用いた。主な層別化因子である 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，最初にランダム化された投与群に基づきウパダシチニブ各用量群とアダリムマブ群を比較した。X 線画像データの 2 値変数については，線形外挿で補完した AO データを用いて解析した。線形外挿解析では，主な層別化因子である DMARD の現在の使用の有無で調整した CMH 検定を用いて，最初にランダム化された投与群に基づきウパダシチニブ各用量群とプラセボ併合群を比較した。各 2 値変数について，反応率の点推定値，正規近似に基づく 95%信頼区間及び投与群間差に関する名目 *P* 値を示した。

連続変数について，各投与群の最小二乗平均値及び 95%信頼区間を示した。X 線画像データ以外の連続変数の解析では，AO データを用いて治療，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最初にランダム化された投与群に基づきウパダシチニブ各用量群とアダリムマブ群を比較した。X 線画像データの連続変数については，線形外挿で補完した AO データを用いて解析した。線形外挿解析では，治療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共変量とする共分散分析（ANCOVA）モデルを用いて，最初にランダム化された投与群に基づきウパダシチニブ各用量群とプラセボ併合群を比較した。各連続変数について，反応率の点推定値，正規近似に基づく 95%信頼区間及び投与群間差に関する名目 *P* 値を示した。

感度分析として，ベースライン及びベースライン以降の測定値を含め，SHS 測定値を応答変数として用いたランダム係数モデルを適用した。

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：

長期安全性解析（20[redacted]年[redacted]月[redacted]日の CSR W56 のデータカットオフ日まで）を実施した。

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。有害事象の 100 人年あたりの発現件数は，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及び一覧を，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。安全性データの欠測値は補完しなかった。

要約 / 結論：

有効性の結果：

24 週間治験総括報告書（以下「CSR W24」）の報告と同様に，non-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）の有効性が示された。以下に示す乾癬性関節炎の臨床症状に関連する評価項目について，プラセボと比較して統計学的に有意な改善が認められた：1）筋骨格系症状（関節炎，腱付着部炎，指趾炎及び脊椎炎），2）関節の構造的損傷，3）乾癬の皮膚症状，4）身体機能，5）生活の質及びその他の患者報告アウトカム。MDA を達成した被験者の割合から算出した包括的な疾患コントロールについても，プラセボと比較して統計学的に有意な改善が認められた。更に，乾癬性関節炎の臨床症状に関連するすべての評価項目及び MDA について，ウパダシチニブ 15 mg 及び 30 mg は標準治療（アダリムマブ）と比較して高い又は同程度の有効性を示した。

56 週間の長期有効性の解析において，投与 24 週時に認められたウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）の有効性は，投与 56 週時まで更に改善するか改善が持続した。投与 24 週時にプラセボからウパダシチニブ投与に切り替えた被験者では，投与 1 日時からウパダシチニブ投与を開始した被験者と同様の経時的な改善を示し，投与 56 週時には同程度の改善を示した。投与 56 週時の ACR20 / 50 / 70 反応率は，ウパダシチニブ 15 mg 群でそれぞれ 85.9%，68.2%及び 45.8%，ウパダシチニブ 30 mg 群でそれぞれ 87.2%，70.4%及び 50.4%，プラセボ→ウパダシチニブ 15 mg 群でそれぞれ 87.6%，64.4%及び 34.8%，プラセボ→ウパダシチニブ 30 mg 群でそれぞれ 86.8%，70.3%及び 40.6%であった。

投与 56 週時までに評価したすべての評価項目について，ウパダシチニブ 15 mg と 30 mg で同様の改善を示し，投与 1 日時からウパダシチニブ投与を開始した被験者及び投与 24 週時にウパダシチニブ投与に切り替えた被験者のいずれも，同様の改善を示した。

ウパダシチニブ 15 mg 及び 30 mg の投与では，アダリムマブ投与と比較して投与 24 週時から投与 56 週時まで同程度又は大きな改善を示した。

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 6.92～32.9 ng/mL，30 mg（1 日 1 回）では 11.9～60.1 ng/mL であった。ウパダシチニブ濃度の実測値は，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）の投与では，忍容性は良好であった。曝露期間の中央値は，全ウパダシチニブ 15 mg 群で 486 日（範囲 1～1083 日）及び全ウパダシチニブ 30 mg 群で 486 日（範囲 1～1045 日）であった。本中間解析で観察されたウパダシチニブの安全性プロファイルは，既存の安全性評価と同様であった。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。

- 有害事象及び重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群とアダリムマブ群で同程度であり，全ウパダシチニブ 30 mg 群で多かった。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，全ウパダシチニブ 15 mg 群で最も少なく，全ウパダシチニブ 30 mg 群とアダリムマブ群で同様であった。
- 多く認められた有害事象（いずれかの投与群で 10 件/100 人年以上）は，上気道感染，血中クレアチン

ホスホキナーゼ（以下「CPK」）増加及び上咽頭炎であった。

- 多く認められた特に注目すべき有害事象（いずれかの投与群で 5 件/100 人年超）は，全ウパダシチニブ 15 mg 群で薬物性肝障害及び CPK 増加，全ウパダシチニブ 30 mg 群で薬物性肝障害，CPK 増加，帯状疱疹，好中球減少症及び貧血であった。重篤な感染症，帯状疱疹，貧血，好中球減少症及び CPK 増加の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群と比較して全ウパダシチニブ 30 mg 群の方が多かった。アダリムマブ群との比較では，重篤な感染症，帯状疱疹，貧血，リンパ球減少症及び CPK 増加の 100 人年あたりの発現件数はウパダシチニブの両用量群の方が多く，好中球減少症は全ウパダシチニブ 30 mg 群で多かった。
  - 重篤な感染症の 100 人年あたりの発現件数は，全ウパダシチニブ 30 mg 群，全ウパダシチニブ 15 mg 群，アダリムマブ群の順に多かった。基本語別でいずれかの投与群で 3 件以上発現した重篤な感染症は，肺炎（全ウパダシチニブ 30 mg 群で 8 件，全ウパダシチニブ 15 mg 群で 6 件），帯状疱疹（全ウパダシチニブ 30 mg 群で 4 件），虫垂炎及び気管支炎（全ウパダシチニブ 30 mg 群で各 3 件），蜂巣炎（アダリムマブ群で 3 件）のみであった。日和見感染（結核及び帯状疱疹を除く）の発現は少なく（1.0 件/100 人年以下），全ウパダシチニブ 15 mg 群及び全ウパダシチニブ 30 mg 群のみで発現した。
  - 帯状疱疹の多くは，重症度が軽度又は中等度で，非重篤で非播種性（皮膚分節が 1～2 箇所に限定）であり，治験薬の投与中止には至らなかった。メディカルレビューの結果，中枢神経系又は皮膚以外に発現した帯状疱疹は認められなかった。
  - 消化管穿孔は，全ウパダシチニブ 15 mg 群で 2 件（穿孔性胃潰瘍及び腸膀胱瘻）認められた。いずれの事象も治験薬と関連なしと判断され，その他の原因として，穿孔性胃潰瘍では非ステロイド系抗炎症薬とメトトレキサートの併用投与，腸膀胱瘻では憩室症が考えられた。
  - 薬物性肝障害の多くは ALT 及び AST 増加であった。重篤な薬物性肝障害は 3 件（全ウパダシチニブ 30 mg 群で 1 件及びアダリムマブ群で 2 件）認められたが，薬物性肝障害の多くは非重篤であり，治験薬の投与中止には至らなかった。グレード 3 又は 4 の ALT 又は AST 増加の発現は少なく，多くは単発のものであった。Hy’s law に該当した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，重症度が軽度であった。貧血及びリンパ球減少症の多くは治験薬の投与中止には至らず，好中球減少症では治験薬の投与中止に至った被験者は認められなかった。グレード 3 以上の血液学的検査値は，おおむね頻度が低く，一過性のものであった。
  - CPK 増加はいずれも非重篤であった。多くの事象は重症度が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。横紋筋融解症が認められた被験者はいなかった。グレード 3 以上の CPK 増加の発現割合は，全ウパダシチニブ 30 mg 群で最も高かった。
  - 悪性腫瘍の 100 人年あたりの発現被験者数は少なく，各投与群で同様であった（全ウパダシチニブ 15 mg 群で 1.1 名/100 人年，全ウパダシチニブ 30 mg 群で 1.3 名/100 人年，アダリムマブ群で 1.0 名/100 人年，以下，同順で記載）。100 人年あたりの発現被験者数は，非黒色腫皮膚癌（以下「NMSC」）で 0.6 名/100 人年，0.6 名/100 人年及び 0.3 名/100 人年，悪性腫瘍（NMSC を除く）で 0.6 名/100 人年，0.7 名/100 人年及び 0.6 名/100 人年であった。リンパ腫は認められなかった。前立腺癌が認められなかった以外は，悪性腫瘍の種類は乾癬性関節炎患者集団でよく認められるものと同様であった。
  - 主要心血管イベント（以下「MACE」）及び静脈血栓塞栓症（以下「VTE」）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 群，30 mg 群及びアダリムマブ群（以下，同順で記載）で同様であり，MACE で 0.4 名/100 人年，0.2 名/100 人年及び 0.5 名/100 人年，VTE で 0.4 名/100 人年，0.5 名/100 人年及び 0.3 名/100 人年であった。
  - 死亡に至った有害事象は 3 件報告された。プラセボ→ウパダシチニブ 30 mg 群の 1 名はコロナウイルス感染（ウパダシチニブ 30 mg 投与に切替え後 788 日で発現）により死亡し，アダリムマブ群の 1 名は自動車事故に遭い，多発性外傷のため死亡した。プラセボ群の 1 名は心停止により死亡し，原因未特定 / 不明の死亡と判定された。また，評価期間以降の死亡（ウパダシチニブの最終投与 30 日後より後に発現）が 3 件報告された。ウパダシチニブ 15 mg 群では，1 名が遠隔転移を伴う肺癌によ

り死亡し，別の 1 名はコロナウイルス感染と考えられる下気道感染により死亡した。ウパダシチニブ 30 mg 群の 1 名は間質性肺疾患により死亡した。

- 活動性結核は，いずれの投与群でも報告されなかった。

- いずれの投与群でも，体重増加を除き，バイタルサインに重要な変化は認められなかった。

結論：

non-bDMARD-IR の中等症から重症の活動性乾癬性関節炎患者において，CSR W24 で報告されたウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）の有効性は，筋骨格症状及び乾癬性皮膚症状，身体機能，疲労及びその他の患者報告アウトカム，乾癬性関節炎の疾患活動性の包括的評価指標，並びに X 線画像上の疾患進行の抑制で，投与 56 週時まで改善が持続又は更に改善した。ウパダシチニブを 56 週間投与したときの改善は，15 mg 及び 30 mg で同程度であった。投与 24 週時にプラセボからウパダシチニブ投与に切り替えた被験者では，投与 1 日時からウパダシチニブ投与を開始した被験者と同様の経時的な改善を示し，投与 56 週時では同程度の改善を示した。ウパダシチニブ 15 mg 及び 30 mg の投与では，アダリムマブ投与と比較して投与 24 週時から投与 56 週時まで同程度又は大きな改善を示した。

安全性では，ウパダシチニブ 15 mg 及び 30 mg（いずれも 1 日 1 回）の長期投与時（平均値約 500 日）の忍容性はおおむね良好であった。有効性及び安全性の結果より，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 56 週時カットオフまでの有害事象の 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：M15-572 試験 CSR W56 Table 14.3__1.2

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 2359 (281.1) | 2814 (333.9) | 1679 (265.9) |
| 血液およびリンパ系障害 | 98 (11.7) | 165 (19.6) | 50 (7.9) |
| 貧血 | 13 (1.5) | 27 (3.2) | 3 (0.5) |
| 大球性貧血 | 2 (0.2) | 4 (0.5) | 0 |
| 慢性疾患の貧血 | 1 (0.1) | 0 | 0 |
| 自己免疫性貧血 | 0 | 2 (0.2) | 0 |
| 好塩基球増加症 | 0 | 1 (0.1) | 0 |
| 失血性貧血 | 0 | 1 (0.1) | 0 |
| 骨髄浮腫 | 0 | 1 (0.1) | 0 |
| 好酸球増加症 | 0 | 1 (0.1) | 1 (0.2) |
| 赤血球減少症 | 0 | 3 (0.4) | 0 |
| 顆粒球減少症 | 0 | 3 (0.4) | 0 |
| 高色素性貧血 | 0 | 0 | 1 (0.2) |
| 内出血発生の増加傾向 | 3 (0.4) | 1 (0.1) | 2 (0.3) |
| 鉄欠乏性貧血 | 2 (0.2) | 2 (0.2) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 血液およびリンパ系障害 (Cont.) | | | |
| 白血球増加症 | 0 | 3 (0.4) | 1 (0.2) |
| 白血球減少症 | 27 (3.2) | 34 (4.0) | 11 (1.7) |
| リンパ節症 | 3 (0.4) | 2 (0.2) | 1 (0.2) |
| リンパ球増加症 | 0 | 1 (0.1) | 0 |
| リンパ組織過形成 | 0 | 1 (0.1) | 0 |
| リンパ球減少症 | 22 (2.6) | 26 (3.1) | 1 (0.2) |
| 大赤血球症 | 0 | 0 | 1 (0.2) |
| 単球増加症 | 1 (0.1) | 0 | 0 |
| 好中球減少症 | 18 (2.1) | 37 (4.4) | 21 (3.3) |
| 好中球増加症 | 2 (0.2) | 4 (0.5) | 2 (0.3) |
| 正色素性貧血 | 0 | 1 (0.1) | 0 |
| 正色素性正球性貧血 | 0 | 0 | 2 (0.3) |
| 血小板減少症 | 3 (0.4) | 5 (0.6) | 2 (0.3) |
| 血小板増加症 | 1 (0.1) | 5 (0.6) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 心臓障害 | 24 (2.9) | 29 (3.4) | 24 (3.8) |
| 急性心筋梗塞 | 0 | 0 | 1 (0.2) |
| 狭心症 | 1 (0.1) | 2 (0.2) | 2 (0.3) |
| 大動脈弁硬化症 | 2 (0.2) | 0 | 0 |
| 不整脈 | 0 | 1 (0.1) | 0 |
| 冠動脈硬化症 | 0 | 1 (0.1) | 2 (0.3) |
| 心房細動 | 3 (0.4) | 5 (0.6) | 2 (0.3) |
| 心房粗動 | 0 | 2 (0.2) | 0 |
| 房室ブロック | 0 | 1 (0.1) | 1 (0.2) |
| 第一度房室ブロック | 1 (0.1) | 0 | 0 |
| 第二度房室ブロック | 0 | 1 (0.1) | 0 |
| 徐脈 | 0 | 0 | 1 (0.2) |
| 左脚ブロック | 0 | 0 | 1 (0.2) |
| 右脚ブロック | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 心不全 | 1 (0.1) | 1 (0.1) | 0 |
| うっ血性心不全 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 心臓障害 (Cont.) | | | |
| 心室血栓症 | 0 | 0 | 1 (0.2) |
| 冠動脈疾患 | 0 | 2 (0.2) | 1 (0.2) |
| チアノーゼ | 0 | 1 (0.1) | 0 |
| 期外収縮 | 2 (0.2) | 1 (0.1) | 0 |
| 左室機能不全 | 0 | 0 | 1 (0.2) |
| 僧帽弁疾患 | 0 | 0 | 1 (0.2) |
| 僧帽弁閉鎖不全症 | 1 (0.1) | 0 | 0 |
| 僧帽弁硬化症 | 1 (0.1) | 0 | 0 |
| 心筋梗塞 | 1 (0.1) | 2 (0.2) | 0 |
| 心筋虚血 | 1 (0.1) | 0 | 2 (0.3) |
| 動悸 | 5 (0.6) | 1 (0.1) | 0 |
| 心膜炎 | 0 | 0 | 1 (0.2) |
| 肺動脈弁閉鎖不全症 | 2 (0.2) | 0 | 0 |
| 洞性徐脈 | 0 | 2 (0.2) | 1 (0.2) |
| 洞性頻脈 | 0 | 1 (0.1) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 心臓障害 (Cont.) | | | |
| 上室性頻脈 | 0 | 0 | 1 (0.2) |
| 頻脈 | 1 (0.1) | 2 (0.2) | 2 (0.3) |
| 発作性頻脈 | 0 | 1 (0.1) | 0 |
| 三尖弁閉鎖不全症 | 1 (0.1) | 0 | 0 |
| 心室性期外収縮 | 0 | 0 | 1 (0.2) |
| 先天性、家族性および遺伝性障害 | 4 (0.5) | 2 (0.2) | 0 |
| 発育性股関節形成不全 | 1 (0.1) | 0 | 0 |
| 陰嚢水瘤 | 3 (0.4) | 1 (0.1) | 0 |
| 2a型高脂血症 | 0 | 1 (0.1) | 0 |
| 耳および迷路障害 | 8 (1.0) | 8 (0.9) | 6 (1.0) |
| 耳垢栓塞 | 0 | 2 (0.2) | 0 |
| 耳閉 | 0 | 1 (0.1) | 1 (0.2) |
| 耳痛 | 0 | 1 (0.1) | 0 |
| 外耳の炎症 | 1 (0.1) | 0 | 0 |
| 耳鳴 | 2 (0.2) | 0 | 3 (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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 耳および迷路障害 (Cont.) | | | |
| 回転性めまい | 3 (0.4) | 1 (0.1) | 2 (0.3) |
| 頭位性回転性めまい | 2 (0.2) | 2 (0.2) | 0 |
| 前庭障害 | 0 | 1 (0.1) | 0 |
| 内分泌障害 | 6 (0.7) | 5 (0.6) | 1 (0.2) |
| 副腎石灰化 | 0 | 1 (0.1) | 0 |
| アンドロゲン欠乏症 | 1 (0.1) | 0 | 0 |
| 自己免疫性甲状腺炎 | 1 (0.1) | 0 | 0 |
| 甲状腺腫 | 2 (0.2) | 1 (0.1) | 1 (0.2) |
| 甲状腺機能亢進症 | 1 (0.1) | 1 (0.1) | 0 |
| 甲状腺機能低下症 | 1 (0.1) | 1 (0.1) | 0 |
| 甲状腺腫瘤 | 0 | 1 (0.1) | 0 |
| 眼障害 | 26 (3.1) | 31 (3.7) | 15 (2.4) |
| 動脈硬化性網膜症 | 1 (0.1) | 0 | 0 |
| 眼瞼炎 | 0 | 0 | 1 (0.2) |
| 眼瞼痙攣 | 1 (0.1) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 眼障害 (Cont.) | | | |
| 境界域緑内障 | 1 (0.1) | 0 | 0 |
| 白内障 | 2 (0.2) | 9 (1.1) | 4 (0.6) |
| 核性白内障 | 0 | 1 (0.1) | 0 |
| 霰粒腫 | 0 | 2 (0.2) | 0 |
| 結膜出血 | 1 (0.1) | 0 | 1 (0.2) |
| 結膜充血 | 1 (0.1) | 0 | 0 |
| アレルギー性結膜炎 | 0 | 1 (0.1) | 0 |
| 角膜混濁 | 0 | 1 (0.1) | 0 |
| 眼瞼皮膚弛緩症 | 0 | 1 (0.1) | 0 |
| 糖尿病網膜症 | 1 (0.1) | 0 | 1 (0.2) |
| 複視 | 0 | 1 (0.1) | 0 |
| ドライアイ | 0 | 1 (0.1) | 0 |
| 眼痛 | 1 (0.1) | 2 (0.2) | 0 |
| 眼瞼下垂 | 2 (0.2) | 1 (0.1) | 0 |
| 緑内障 | 2 (0.2) | 5 (0.6) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 眼障害 (Cont.) | | | |
| 虹彩毛様体炎 | 0 | 1 (0.1) | 0 |
| 角膜炎 | 0 | 1 (0.1) | 1 (0.2) |
| 流涙増加 | 0 | 1 (0.1) | 0 |
| 瞼板腺炎 | 1 (0.1) | 0 | 1 (0.2) |
| 眼部不快感 | 0 | 1 (0.1) | 0 |
| 眼窩周囲浮腫 | 0 | 0 | 2 (0.3) |
| 眼窩周囲腫脹 | 0 | 1 (0.1) | 0 |
| 光視症 | 1 (0.1) | 0 | 0 |
| 翼状片 | 0 | 0 | 1 (0.2) |
| 眼瞼腫脹 | 1 (0.1) | 0 | 0 |
| ぶどう膜炎 | 1 (0.1) | 0 | 1 (0.2) |
| 霧視 | 3 (0.4) | 0 | 2 (0.3) |
| 視力低下 | 0 | 1 (0.1) | 0 |
| 視力障害 | 4 (0.5) | 0 | 0 |
| 硝子体剥離 | 1 (0.1) | 0 | 0 |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 眼障害 (Cont.) | | | |
| 硝子体浮遊物 | 1 (0.1) | 0 | 0 |
| 胃腸障害 | 200 (23.8) | 206 (24.4) | 160 (25.3) |
| 腹部不快感 | 3 (0.4) | 3 (0.4) | 3 (0.5) |
| 腹部膨満 | 2 (0.2) | 3 (0.4) | 1 (0.2) |
| 腹部腫瘤 | 1 (0.1) | 0 | 0 |
| 腹痛 | 8 (1.0) | 5 (0.6) | 6 (1.0) |
| 下腹部痛 | 2 (0.2) | 0 | 3 (0.5) |
| 上腹部痛 | 13 (1.5) | 9 (1.1) | 7 (1.1) |
| 腹壁嚢胞 | 0 | 1 (0.1) | 0 |
| 裂肛 | 0 | 1 (0.1) | 0 |
| 痔瘻 | 0 | 1 (0.1) | 0 |
| 口角口唇炎 | 1 (0.1) | 1 (0.1) | 0 |
| アフタ性潰瘍 | 2 (0.2) | 3 (0.4) | 1 (0.2) |
| 根尖肉芽腫 | 0 | 1 (0.1) | 0 |
| 腹水 | 0 | 0 | 1 (0.2) |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 慢性胃炎 | 2 (0.2) | 2 (0.2) | 0 |
| 大腸炎 | 2 (0.2) | 0 | 0 |
| 結腸異形成 | 1 (0.1) | 0 | 0 |
| 便秘 | 4 (0.5) | 5 (0.6) | 8 (1.3) |
| 齲歯 | 2 (0.2) | 3 (0.4) | 1 (0.2) |
| 横隔膜ヘルニア | 1 (0.1) | 0 | 0 |
| 下痢 | 35 (4.2) | 36 (4.3) | 25 (4.0) |
| 憩室 | 4 (0.5) | 2 (0.2) | 1 (0.2) |
| 腸憩室 | 0 | 2 (0.2) | 2 (0.3) |
| 食道憩室 | 0 | 1 (0.1) | 0 |
| 後天性過長結腸 | 0 | 0 | 1 (0.2) |
| 口内乾燥 | 0 | 2 (0.2) | 2 (0.3) |
| 十二指腸潰瘍 | 0 | 2 (0.2) | 2 (0.3) |
| 出血性十二指腸潰瘍 | 0 | 1 (0.1) | 0 |
| 十二指腸炎 | 0 | 2 (0.2) | 0 |

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Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 排便困難 | 0 | 1 (0.1) | 0 |
| 消化不良 | 9 (1.1) | 6 (0.7) | 4 (0.6) |
| 嚥下障害 | 0 | 2 (0.2) | 0 |
| 小腸炎 | 2 (0.2) | 2 (0.2) | 2 (0.3) |
| 腸炎 | 0 | 2 (0.2) | 0 |
| 腸膀胱瘻 | 1 (0.1) | 0 | 0 |
| 心窩部不快感 | 1 (0.1) | 0 | 1 (0.2) |
| びらん性十二指腸炎 | 1 (0.1) | 0 | 0 |
| びらん性食道炎 | 0 | 1 (0.1) | 0 |
| おくび | 1 (0.1) | 0 | 0 |
| 糞塊 | 0 | 1 (0.1) | 0 |
| 鼓腸 | 1 (0.1) | 3 (0.4) | 2 (0.3) |
| 食中毒 | 2 (0.2) | 2 (0.2) | 3 (0.5) |
| 胃ポリープ | 0 | 0 | 1 (0.2) |
| 胃潰瘍 | 0 | 0 | 1 (0.2) |

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Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 穿孔性胃潰瘍 | 1 (0.1) | 0 | 0 |
| 胃炎 | 9 (1.1) | 8 (0.9) | 5 (0.8) |
| びらん性胃炎 | 3 (0.4) | 1 (0.1) | 2 (0.3) |
| 胃十二指腸出血 | 1 (0.1) | 0 | 0 |
| 胃十二指腸潰瘍 | 0 | 1 (0.1) | 0 |
| 胃腸出血 | 1 (0.1) | 0 | 1 (0.2) |
| 胃食道逆流性疾患 | 8 (1.0) | 9 (1.1) | 6 (1.0) |
| 歯肉退縮 | 0 | 0 | 1 (0.2) |
| 歯肉腫脹 | 0 | 1 (0.1) | 0 |
| 舌炎 | 1 (0.1) | 0 | 0 |
| 血便排泄 | 2 (0.2) | 1 (0.1) | 1 (0.2) |
| 痔核 | 2 (0.2) | 2 (0.2) | 2 (0.3) |
| 裂孔ヘルニア | 3 (0.4) | 3 (0.4) | 2 (0.3) |
| 鼠径ヘルニア | 0 | 1 (0.1) | 1 (0.2) |
| 腸閉塞 | 1 (0.1) | 0 | 0 |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 腸管ポリープ | 0 | 0 | 1 (0.2) |
| 過敏性腸症候群 | 0 | 0 | 1 (0.2) |
| 大腸ポリープ | 3 (0.4) | 0 | 3 (0.5) |
| 口腔内白斑症 | 0 | 0 | 1 (0.2) |
| 口唇乾燥 | 1 (0.1) | 0 | 0 |
| 口唇潰瘍 | 1 (0.1) | 1 (0.1) | 0 |
| メレナ | 0 | 0 | 2 (0.3) |
| 口腔嚢胞 | 0 | 1 (0.1) | 0 |
| 口腔内潰瘍形成 | 4 (0.5) | 10 (1.2) | 1 (0.2) |
| 悪心 | 18 (2.1) | 26 (3.1) | 24 (3.8) |
| 嚥下痛 | 0 | 1 (0.1) | 0 |
| 食道痙攣 | 0 | 1 (0.1) | 0 |
| 食道潰瘍 | 0 | 1 (0.1) | 0 |
| 食道潰瘍出血 | 1 (0.1) | 0 | 0 |
| 食道炎 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 口腔挫傷 | 1 (0.1) | 0 | 0 |
| 口腔粘膜びらん | 0 | 1 (0.1) | 0 |
| 口腔粘膜水疱形成 | 0 | 1 (0.1) | 0 |
| 膵臓障害 | 1 (0.1) | 0 | 1 (0.2) |
| 膵腫瘤 | 0 | 1 (0.1) | 0 |
| 膵脂肪変性 | 0 | 1 (0.1) | 0 |
| 膵炎 | 1 (0.1) | 0 | 0 |
| 慢性膵炎 | 1 (0.1) | 1 (0.1) | 0 |
| 耳下腺腫大 | 0 | 1 (0.1) | 0 |
| 消化性潰瘍 | 1 (0.1) | 0 | 2 (0.3) |
| 歯周の炎症 | 1 (0.1) | 0 | 0 |
| 直腸出血 | 1 (0.1) | 2 (0.2) | 0 |
| 逆流性胃炎 | 1 (0.1) | 0 | 0 |
| 吐き戻し | 0 | 1 (0.1) | 0 |
| レッチング | 1 (0.1) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 流涎過多 | 0 | 0 | 1 (0.2) |
| 口内炎 | 4 (0.5) | 6 (0.7) | 1 (0.2) |
| ストレス潰瘍 | 0 | 0 | 1 (0.2) |
| 舌障害 | 0 | 0 | 1 (0.2) |
| 舌潰瘍 | 1 (0.1) | 2 (0.2) | 0 |
| 変色歯 | 0 | 0 | 1 (0.2) |
| 歯の障害 | 1 (0.1) | 1 (0.1) | 0 |
| 歯の脱落 | 1 (0.1) | 0 | 1 (0.2) |
| 歯痛 | 7 (0.8) | 2 (0.2) | 1 (0.2) |
| 上部消化管出血 | 1 (0.1) | 1 (0.1) | 0 |
| 嘔吐 | 15 (1.8) | 11 (1.3) | 17 (2.7) |
| 一般・全身障害および投与部位の状態 | 57 (6.8) | 79 (9.4) | 92 (14.6) |
| 医薬品副作用 | 1 (0.1) | 0 | 1 (0.2) |
| 無力症 | 3 (0.4) | 4 (0.5) | 0 |
| 胸痛 | 4 (0.5) | 3 (0.4) | 4 (0.6) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 一般・全身障害および投与部位の状態 (Cont.) | | | |
| 悪寒 | 1 (0.1) | 1 (0.1) | 0 |
| 不快感 | 1 (0.1) | 0 | 0 |
| 薬物不耐性 | 2 (0.2) | 3 (0.4) | 0 |
| 粘膜疹 | 0 | 1 (0.1) | 0 |
| 顔面痛 | 0 | 2 (0.2) | 0 |
| 疲労 | 13 (1.5) | 8 (0.9) | 11 (1.7) |
| 歩行障害 | 0 | 2 (0.2) | 0 |
| 高熱 | 1 (0.1) | 0 | 0 |
| 低体温 | 0 | 1 (0.1) | 0 |
| 治癒不良 | 0 | 1 (0.1) | 0 |
| 炎症 | 0 | 1 (0.1) | 2 (0.3) |
| インフルエンザ様疾患 | 4 (0.5) | 4 (0.5) | 2 (0.3) |
| 注射部位内出血 | 0 | 1 (0.1) | 3 (0.5) |
| 注射部位湿疹 | 0 | 0 | 3 (0.5) |
| 注射部位紅斑 | 0 | 0 | 5 (0.8) |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 一般・全身障害および投与部位の状態 (Cont.) | | | |
| 注射部位過敏反応 | 0 | 0 | 1 (0.2) |
| 注射部位硬結 | 0 | 0 | 1 (0.2) |
| 注射部位疼痛 | 0 | 1 (0.1) | 5 (0.8) |
| 注射部位そう痒感 | 0 | 0 | 2 (0.3) |
| 注射部位反応 | 0 | 2 (0.2) | 24 (3.8) |
| 注射部位蕁麻疹 | 0 | 0 | 3 (0.5) |
| 倦怠感 | 4 (0.5) | 0 | 2 (0.3) |
| 小結節 | 0 | 1 (0.1) | 1 (0.2) |
| 非心臓性胸痛 | 0 | 1 (0.1) | 0 |
| 浮腫 | 1 (0.1) | 0 | 0 |
| 末梢性浮腫 | 7 (0.8) | 6 (0.7) | 9 (1.4) |
| 疼痛 | 2 (0.2) | 3 (0.4) | 2 (0.3) |
| 末梢腫脹 | 4 (0.5) | 4 (0.5) | 2 (0.3) |
| 発熱 | 9 (1.1) | 27 (3.2) | 7 (1.1) |
| 軟部組織の炎症 | 0 | 1 (0.1) | 0 |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 一般・全身障害および投与部位の状態 (Cont.) | | | |
| 腫脹 | 0 | 1 (0.1) | 0 |
| 口渇 | 0 | 0 | 1 (0.2) |
| ワクチン接種部位そう痒感 | 0 | 0 | 1 (0.2) |
| 肝胆道系障害 | 36 (4.3) | 43 (5.1) | 34 (5.4) |
| 胆管結石 | 0 | 1 (0.1) | 0 |
| 胆道仙痛 | 1 (0.1) | 0 | 0 |
| 胆道ジスキネジア | 0 | 0 | 1 (0.2) |
| 胆嚢炎 | 1 (0.1) | 2 (0.2) | 0 |
| 慢性胆嚢炎 | 0 | 1 (0.1) | 1 (0.2) |
| 胆石症 | 5 (0.6) | 4 (0.5) | 3 (0.5) |
| 薬物性肝障害 | 0 | 1 (0.1) | 4 (0.6) |
| 肝嚢胞 | 0 | 1 (0.1) | 1 (0.2) |
| 肝線維症 | 0 | 0 | 1 (0.2) |
| 肝機能異常 | 12 (1.4) | 12 (1.4) | 3 (0.5) |
| 肝腫瘤 | 0 | 1 (0.1) | 0 |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 肝胆道系障害 (Cont.) | | | |
| 脂肪肝 | 7 (0.8) | 11 (1.3) | 10 (1.6) |
| 肝炎 | 1 (0.1) | 1 (0.1) | 0 |
| 肝腫大 | 0 | 1 (0.1) | 2 (0.3) |
| 肝毒性 | 1 (0.1) | 1 (0.1) | 0 |
| 高ビリルビン血症 | 1 (0.1) | 1 (0.1) | 0 |
| 高トランスアミナーゼ血症 | 0 | 1 (0.1) | 2 (0.3) |
| 黄疸 | 0 | 0 | 1 (0.2) |
| 肝障害 | 2 (0.2) | 2 (0.2) | 3 (0.5) |
| 肝損傷 | 0 | 0 | 1 (0.2) |
| 非アルコール性脂肪性肝炎 | 2 (0.2) | 0 | 0 |
| 非アルコール性脂肪性肝疾患 | 1 (0.1) | 2 (0.2) | 0 |
| 門脈血栓症 | 0 | 0 | 1 (0.2) |
| 脂肪性肝炎 | 2 (0.2) | 0 | 0 |
| 免疫系障害 | 8 (1.0) | 10 (1.2) | 6 (1.0) |
| 節足動物咬傷アレルギー | 0 | 2 (0.2) | 0 |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 免疫系障害 (Cont.) | | | |
| 薬物過敏症 | 1 (0.1) | 1 (0.1) | 0 |
| 食物アレルギー | 2 (0.2) | 1 (0.1) | 0 |
| 過敏症 | 1 (0.1) | 1 (0.1) | 4 (0.6) |
| 免疫系障害 | 0 | 1 (0.1) | 0 |
| ダニアレルギー | 0 | 2 (0.2) | 0 |
| 季節性アレルギー | 4 (0.5) | 2 (0.2) | 2 (0.3) |
| 感染症および寄生虫症 | 777 (92.6) | 945 (112.1) | 442 (70.0) |
| 腹部膿瘍 | 0 | 2 (0.2) | 0 |
| 腹壁膿瘍 | 1 (0.1) | 0 | 0 |
| 四肢膿瘍 | 0 | 4 (0.5) | 1 (0.2) |
| 口腔膿瘍 | 0 | 1 (0.1) | 0 |
| ダニ皮膚炎 | 1 (0.1) | 0 | 0 |
| 急性副鼻腔炎 | 3 (0.4) | 1 (0.1) | 2 (0.3) |
| 歯槽骨炎 | 0 | 0 | 1 (0.2) |
| 肛門膿瘍 | 0 | 1 (0.1) | 0 |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 虫垂炎 | 1 (0.1) | 3 (0.4) | 0 |
| 細菌性関節炎 | 1 (0.1) | 0 | 0 |
| 無症候性細菌尿 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 異型肺炎 | 0 | 2 (0.2) | 0 |
| バベシア症 | 0 | 1 (0.1) | 0 |
| 菌血症 | 0 | 1 (0.1) | 0 |
| 細菌感染 | 1 (0.1) | 0 | 1 (0.2) |
| 細菌性卵管炎 | 0 | 1 (0.1) | 0 |
| 細菌性膣症 | 1 (0.1) | 0 | 1 (0.2) |
| 細菌尿 | 1 (0.1) | 1 (0.1) | 0 |
| 体部白癬 | 2 (0.2) | 3 (0.4) | 0 |
| 骨膿瘍 | 0 | 0 | 1 (0.2) |
| 乳房膿瘍 | 0 | 1 (0.1) | 0 |
| 気管支炎 | 48 (5.7) | 56 (6.6) | 18 (2.9) |
| 細菌性気管支炎 | 1 (0.1) | 1 (0.1) | 0 |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| マイコプラズマ性気管支炎 | 0 | 0 | 1 (0.2) |
| 気管支肺アスペルギルス症 | 1 (0.1) | 0 | 0 |
| 感染性滑液包炎 | 0 | 1 (0.1) | 0 |
| カンジダ感染 | 1 (0.1) | 0 | 0 |
| カンジダ性尿道炎 | 1 (0.1) | 0 | 0 |
| 蜂巣炎 | 5 (0.6) | 4 (0.5) | 11 (1.7) |
| 慢性副鼻腔炎 | 0 | 0 | 2 (0.3) |
| 慢性扁桃炎 | 0 | 0 | 2 (0.3) |
| 結膜炎 | 7 (0.8) | 6 (0.7) | 6 (1.0) |
| ウイルス性結膜炎 | 1 (0.1) | 0 | 0 |
| コロナウイルス感染 | 5 (0.6) | 9 (1.1) | 2 (0.3) |
| 膀胱炎 | 12 (1.4) | 11 (1.3) | 12 (1.9) |
| サイトメガロウイルス感染 | 0 | 1 (0.1) | 0 |
| 毛嚢虫症 | 1 (0.1) | 1 (0.1) | 0 |
| デング熱 | 0 | 1 (0.1) | 0 |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 爪の皮膚糸状菌症 | 1 (0.1) | 0 | 0 |
| 憩室炎 | 3 (0.4) | 0 | 1 (0.2) |
| 耳感染 | 10 (1.2) | 3 (0.4) | 4 (0.6) |
| エンテロウイルス感染 | 1 (0.1) | 0 | 1 (0.2) |
| 丹毒 | 2 (0.2) | 2 (0.2) | 1 (0.2) |
| 紅色陰癬 | 0 | 0 | 4 (0.6) |
| 大腸菌性尿路感染 | 2 (0.2) | 3 (0.4) | 0 |
| 眼感染 | 0 | 0 | 2 (0.3) |
| 熱性感染症 | 1 (0.1) | 0 | 0 |
| 毛包炎 | 13 (1.5) | 8 (0.9) | 2 (0.3) |
| 真菌感染 | 1 (0.1) | 1 (0.1) | 0 |
| 皮膚真菌感染 | 8 (1.0) | 11 (1.3) | 3 (0.5) |
| せつ | 3 (0.4) | 0 | 2 (0.3) |
| ウイルス性胃炎 | 0 | 1 (0.1) | 0 |
| 胃腸炎 | 22 (2.6) | 30 (3.6) | 13 (2.1) |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| ウイルス性胃腸炎 | 2 (0.2) | 15 (1.8) | 6 (1.0) |
| 消化管感染 | 3 (0.4) | 0 | 1 (0.2) |
| ウイルス性消化管感染 | 0 | 1 (0.1) | 0 |
| 性器カンジダ症 | 1 (0.1) | 0 | 0 |
| 陰部ヘルペス | 3 (0.4) | 3 (0.4) | 0 |
| 陰部単純ヘルペス | 2 (0.2) | 0 | 1 (0.2) |
| 陰部帯状疱疹 | 1 (0.1) | 0 | 0 |
| 真菌性性器感染 | 1 (0.1) | 0 | 0 |
| 泌尿生殖器感染 | 1 (0.1) | 0 | 0 |
| 歯肉炎 | 3 (0.4) | 5 (0.6) | 3 (0.5) |
| 肛径部膿瘍 | 0 | 1 (0.1) | 0 |
| H1N1インフルエンザ | 2 (0.2) | 0 | 0 |
| 手足口病 | 1 (0.1) | 0 | 0 |
| ヘリコバクター感染 | 1 (0.1) | 0 | 1 (0.2) |
| B型肝炎 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| B型肝炎再活性化 | 1 (0.1) | 0 | 0 |
| E型肝炎 | 0 | 0 | 1 (0.2) |
| ヘルペス眼感染 | 0 | 1 (0.1) | 0 |
| 単純ヘルペス | 4 (0.5) | 18 (2.1) | 1 (0.2) |
| ヘルペスウイルス感染 | 1 (0.1) | 1 (0.1) | 0 |
| 帯状疱疹 | 29 (3.5) | 49 (5.8) | 3 (0.5) |
| 皮膚播種性帯状疱疹 | 0 | 1 (0.1) | 0 |
| 麦粒腫 | 6 (0.7) | 1 (0.1) | 0 |
| 膿痂疹 | 0 | 1 (0.1) | 0 |
| 咬傷感染 | 0 | 0 | 1 (0.2) |
| 伝染性単核症 | 0 | 1 (0.1) | 0 |
| インフルエンザ | 27 (3.2) | 25 (3.0) | 5 (0.8) |
| 注射部位感染 | 1 (0.1) | 0 | 0 |
| 関節膿瘍 | 0 | 1 (0.1) | 0 |
| クレブシエラ感染 | 1 (0.1) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 喉頭炎 | 5 (0.6) | 7 (0.8) | 1 (0.2) |
| 潜伏結核 | 17 (2.0) | 9 (1.1) | 7 (1.1) |
| 限局性感染 | 3 (0.4) | 2 (0.2) | 2 (0.3) |
| 下気道感染 | 5 (0.6) | 6 (0.7) | 5 (0.8) |
| 肺感染 | 1 (0.1) | 3 (0.4) | 0 |
| ライム病 | 0 | 0 | 2 (0.3) |
| リンパ管炎 | 0 | 1 (0.1) | 0 |
| ムンプス | 1 (0.1) | 0 | 0 |
| 爪床感染 | 0 | 2 (0.2) | 0 |
| 爪感染 | 1 (0.1) | 5 (0.6) | 0 |
| 鼻ヘルペス | 0 | 2 (0.2) | 2 (0.3) |
| 上咽頭炎 | 72 (8.6) | 84 (10.0) | 67 (10.6) |
| 爪真菌症 | 2 (0.2) | 1 (0.1) | 2 (0.3) |
| 口腔カンジダ症 | 4 (0.5) | 6 (0.7) | 1 (0.2) |
| 口腔真菌感染 | 1 (0.1) | 4 (0.5) | 0 |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 口腔ヘルペス | 20 (2.4) | 57 (6.8) | 17 (2.7) |
| 口腔感染 | 0 | 1 (0.1) | 0 |
| 精巣炎 | 0 | 0 | 1 (0.2) |
| 中咽頭カンジダ症 | 0 | 1 (0.1) | 0 |
| 骨髄炎 | 0 | 0 | 1 (0.2) |
| 外耳炎 | 0 | 3 (0.4) | 1 (0.2) |
| 中耳炎 | 0 | 3 (0.4) | 2 (0.3) |
| 急性中耳炎 | 0 | 3 (0.4) | 2 (0.3) |
| 子宮傍組織炎 | 1 (0.1) | 0 | 0 |
| 爪囲炎 | 4 (0.5) | 4 (0.5) | 3 (0.5) |
| パルボウイルス感染 | 0 | 0 | 1 (0.2) |
| 軟骨膜炎 | 0 | 1 (0.1) | 0 |
| 歯周炎 | 5 (0.6) | 2 (0.2) | 0 |
| 腹膜炎 | 0 | 1 (0.1) | 0 |
| 咽頭炎 | 23 (2.7) | 18 (2.1) | 14 (2.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 細菌性咽頭炎 | 1 (0.1) | 0 | 0 |
| レンサ球菌性咽頭炎 | 2 (0.2) | 1 (0.1) | 1 (0.2) |
| 咽頭扁桃炎 | 2 (0.2) | 1 (0.1) | 0 |
| 毛巣嚢胞 | 1 (0.1) | 0 | 0 |
| ニューモシスチス・イロベチイ肺炎 | 0 | 1 (0.1) | 0 |
| 肺炎 | 16 (1.9) | 10 (1.2) | 9 (1.4) |
| 細菌性肺炎 | 1 (0.1) | 0 | 0 |
| レンサ球菌性肺炎 | 0 | 1 (0.1) | 0 |
| 術後創感染 | 1 (0.1) | 0 | 0 |
| 前立腺感染 | 0 | 1 (0.1) | 0 |
| 歯髄炎 | 6 (0.7) | 0 | 0 |
| 化膿性分泌物 | 0 | 1 (0.1) | 0 |
| 腎盂腎炎 | 0 | 1 (0.1) | 0 |
| 急性腎盂腎炎 | 0 | 4 (0.5) | 0 |
| 膿尿 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 膿疱性皮疹 | 1 (0.1) | 4 (0.5) | 0 |
| 気道感染 | 19 (2.3) | 15 (1.8) | 8 (1.3) |
| ウイルス性気道感染 | 17 (2.0) | 20 (2.4) | 9 (1.4) |
| 鼻炎 | 7 (0.8) | 9 (1.1) | 7 (1.1) |
| サルモネラ症 | 0 | 0 | 1 (0.2) |
| 卵管炎 | 0 | 1 (0.1) | 0 |
| 敗血症 | 2 (0.2) | 0 | 0 |
| 副鼻腔炎 | 21 (2.5) | 23 (2.7) | 15 (2.4) |
| 細菌性副鼻腔炎 | 1 (0.1) | 0 | 0 |
| 皮膚細菌感染 | 1 (0.1) | 1 (0.1) | 0 |
| 皮膚感染 | 3 (0.4) | 4 (0.5) | 4 (0.6) |
| 軟部組織感染 | 0 | 0 | 3 (0.5) |
| ブドウ球菌性菌血症 | 0 | 1 (0.1) | 0 |
| ブドウ球菌感染 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| ブドウ球菌性敗血症 | 0 | 1 (0.1) | 0 |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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

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|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| ブドウ球菌皮膚感染 | 1 (0.1) | 2 (0.2) | 0 |
| 皮下組織膿瘍 | 0 | 2 (0.2) | 0 |
| 股部白癬 | 0 | 0 | 1 (0.2) |
| 白癬感染 | 1 (0.1) | 0 | 1 (0.2) |
| 手白癬 | 0 | 1 (0.1) | 0 |
| 足部白癬 | 5 (0.6) | 7 (0.8) | 3 (0.5) |
| 癜風 | 3 (0.4) | 0 | 1 (0.2) |
| 扁桃炎 | 9 (1.1) | 9 (1.1) | 6 (1.0) |
| 細菌性扁桃炎 | 6 (0.7) | 1 (0.1) | 0 |
| 歯膿瘍 | 8 (1.0) | 3 (0.4) | 2 (0.3) |
| 歯感染 | 3 (0.4) | 9 (1.1) | 4 (0.6) |
| 気管炎 | 3 (0.4) | 3 (0.4) | 0 |
| 気管気管支炎 | 4 (0.5) | 6 (0.7) | 1 (0.2) |
| トリコモナス症 | 0 | 0 | 1 (0.2) |
| トリコフィトン感染症 | 1 (0.1) | 0 | 0 |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 上気道感染 | 124 (14.8) | 152 (18.0) | 73 (11.6) |
| 尿道炎 | 0 | 1 (0.1) | 0 |
| 尿路感染 | 56 (6.7) | 79 (9.4) | 23 (3.6) |
| 細菌性尿路感染 | 0 | 1 (0.1) | 0 |
| 尿路性敗血症 | 0 | 1 (0.1) | 0 |
| 腟感染 | 0 | 1 (0.1) | 3 (0.5) |
| ウイルス血症 | 1 (0.1) | 0 | 0 |
| ウイルス感染 | 4 (0.5) | 10 (1.2) | 3 (0.5) |
| ウイルス性咽頭炎 | 1 (0.1) | 2 (0.2) | 0 |
| ウイルス性発疹 | 1 (0.1) | 0 | 0 |
| ウイルス性副鼻腔炎 | 0 | 1 (0.1) | 0 |
| ウイルス性気管炎 | 2 (0.2) | 1 (0.1) | 0 |
| ウイルス性上気道感染 | 12 (1.4) | 11 (1.3) | 5 (0.8) |
| 外陰部膿瘍 | 0 | 0 | 2 (0.3) |
| 女性外陰部蜂巣炎 | 0 | 0 | 1 (0.2) |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 外陰部炎 | 1 (0.1) | 0 | 0 |
| 外陰部腟カンジダ症 | 4 (0.5) | 4 (0.5) | 1 (0.2) |
| 外陰腟真菌感染 | 4 (0.5) | 11 (1.3) | 2 (0.3) |
| 外陰腟炎 | 1 (0.1) | 2 (0.2) | 0 |
| 創傷感染 | 0 | 0 | 1 (0.2) |
| 傷害、中毒および処置合併症 | 81 (9.7) | 91 (10.8) | 82 (13.0) |
| 偶発的過量投与 | 0 | 0 | 1 (0.2) |
| 動物咬傷 | 1 (0.1) | 2 (0.2) | 0 |
| 足関節部骨折 | 1 (0.1) | 2 (0.2) | 0 |
| 節足動物咬傷 | 4 (0.5) | 2 (0.2) | 4 (0.6) |
| 節足動物刺傷 | 1 (0.1) | 2 (0.2) | 1 (0.2) |
| 剥離骨折 | 0 | 1 (0.1) | 0 |
| 背部損傷 | 1 (0.1) | 0 | 0 |
| 第1度熱傷 | 0 | 1 (0.1) | 0 |
| 軟骨損傷 | 0 | 1 (0.1) | 0 |

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Program Source Code: [redacted]

TABLE 14.3__1.2

Treatment-Emergent Adverse Events per 100 Patient Years
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(Safety Analysis Set)

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|---|---|---|---|
| 傷害、中毒および処置合併症 (Cont.) | | | |
| 鎖骨骨折 | 0 | 1 (0.1) | 0 |
| 粉砕骨折 | 0 | 1 (0.1) | 0 |
| 脳振盪 | 0 | 1 (0.1) | 0 |
| 挫傷 | 9 (1.1) | 8 (0.9) | 9 (1.4) |
| 角膜擦過傷 | 0 | 0 | 1 (0.2) |
| 頭蓋脳損傷 | 0 | 0 | 1 (0.2) |
| 上顆炎 | 0 | 1 (0.1) | 1 (0.2) |
| 転倒 | 4 (0.5) | 8 (0.9) | 12 (1.9) |
| 大腿骨骨折 | 0 | 1 (0.1) | 1 (0.2) |
| 腓骨骨折 | 1 (0.1) | 0 | 1 (0.2) |
| 足骨折 | 4 (0.5) | 2 (0.2) | 0 |
| 前腕骨折 | 0 | 0 | 1 (0.2) |
| 体内異物 | 2 (0.2) | 0 | 0 |
| 眼内異物 | 1 (0.1) | 0 | 0 |
| 仙骨骨折 | 0 | 1 (0.1) | 0 |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 傷害、中毒および処置合併症 (Cont.) | | | |
| 手骨折 | 1 (0.1) | 2 (0.2) | 0 |
| 上腕骨骨折 | 1 (0.1) | 3 (0.4) | 2 (0.3) |
| 腸脛靭帯症候群 | 0 | 0 | 1 (0.2) |
| 注射に伴う反応 | 0 | 0 | 1 (0.2) |
| 損傷 | 0 | 1 (0.1) | 1 (0.2) |
| 角膜損傷 | 0 | 1 (0.1) | 0 |
| 関節脱臼 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 関節損傷 | 4 (0.5) | 3 (0.4) | 4 (0.6) |
| 靭帯損傷 | 0 | 1 (0.1) | 0 |
| 靭帯断裂 | 0 | 2 (0.2) | 1 (0.2) |
| 靭帯捻挫 | 2 (0.2) | 6 (0.7) | 3 (0.5) |
| 四肢損傷 | 5 (0.6) | 0 | 4 (0.6) |
| 口唇損傷 | 0 | 1 (0.1) | 0 |
| 半月板損傷 | 1 (0.1) | 2 (0.2) | 2 (0.3) |
| 多発性外傷 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 傷害、中毒および処置合併症 (Cont.) | | | |
| 筋損傷 | 0 | 1 (0.1) | 0 |
| 筋断裂 | 2 (0.2) | 0 | 0 |
| 肉離れ | 2 (0.2) | 3 (0.4) | 3 (0.5) |
| 骨棘骨折 | 0 | 0 | 1 (0.2) |
| 椎弓切除後症候群 | 0 | 1 (0.1) | 0 |
| 処置後合併症 | 0 | 0 | 1 (0.2) |
| 処置後出血 | 0 | 1 (0.1) | 0 |
| 処置後炎症 | 0 | 0 | 1 (0.2) |
| 外傷後頚部症候群 | 1 (0.1) | 0 | 0 |
| 処置による疼痛 | 1 (0.1) | 1 (0.1) | 0 |
| 恥骨骨折 | 1 (0.1) | 0 | 0 |
| 橈骨骨折 | 1 (0.1) | 2 (0.2) | 1 (0.2) |
| 肋骨骨折 | 1 (0.1) | 2 (0.2) | 0 |
| 交通事故 | 1 (0.1) | 3 (0.4) | 1 (0.2) |
| 引っかき傷 | 1 (0.1) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 傷害、中毒および処置合併症 (Cont.) | | | |
| 皮膚擦過傷 | 2 (0.2) | 1 (0.1) | 4 (0.6) |
| 皮膚裂傷 | 5 (0.6) | 2 (0.2) | 2 (0.3) |
| 皮膚創傷 | 0 | 0 | 1 (0.2) |
| ストレス骨折 | 2 (0.2) | 1 (0.1) | 1 (0.2) |
| サンバーン | 0 | 1 (0.1) | 0 |
| 滑膜断裂 | 1 (0.1) | 0 | 0 |
| 腱損傷 | 0 | 0 | 2 (0.3) |
| 腱断裂 | 0 | 3 (0.4) | 2 (0.3) |
| 熱傷 | 3 (0.4) | 2 (0.2) | 3 (0.5) |
| 脛骨骨折 | 1 (0.1) | 0 | 0 |
| 歯牙破折 | 6 (0.7) | 1 (0.1) | 2 (0.3) |
| 各種物質毒性 | 1 (0.1) | 1 (0.1) | 0 |
| 外傷性骨折 | 0 | 1 (0.1) | 0 |
| 外傷性血腫 | 3 (0.4) | 0 | 0 |
| 上肢骨折 | 0 | 2 (0.2) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 傷害、中毒および処置合併症 (Cont.) | | | |
| 術後尿閉 | 0 | 1 (0.1) | 0 |
| 創傷 | 1 (0.1) | 2 (0.2) | 1 (0.2) |
| 創離開 | 0 | 0 | 1 (0.2) |
| 手首関節骨折 | 1 (0.1) | 1 (0.1) | 0 |
| 臨床検査 | 314 (37.4) | 428 (50.8) | 234 (37.1) |
| アラニンアミノトランスフェラーゼ異常 | 0 | 1 (0.1) | 0 |
| アラニンアミノトランスフェラーゼ増加 | 68 (8.1) | 65 (7.7) | 58 (9.2) |
| アルドラーゼ増加 | 0 | 1 (0.1) | 0 |
| αヒドロキシ酪酸脱水素酵素増加 | 0 | 1 (0.1) | 0 |
| アスパラギン酸アミノトランスフェラーゼ異常 | 0 | 1 (0.1) | 0 |
| アスパラギン酸アミノトランスフェラーゼ増加 | 46 (5.5) | 54 (6.4) | 38 (6.0) |
| 細菌検査陽性 | 1 (0.1) | 1 (0.1) | 0 |
| 血中アルカリホスファターゼ増加 | 2 (0.2) | 0 | 2 (0.3) |
| 血中ビリルビン増加 | 2 (0.2) | 3 (0.4) | 6 (1.0) |
| 血中カルシウム増加 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| 血中コレステロール増加 | 6 (0.7) | 6 (0.7) | 1 (0.2) |
| 血中クレアチンホスホキナーゼ増加 | 100 (11.9) | 146 (17.3) | 46 (7.3) |
| 血中クレアチニン増加 | 6 (0.7) | 8 (0.9) | 3 (0.5) |
| 血中ブドウ糖異常 | 2 (0.2) | 0 | 0 |
| 血中ブドウ糖増加 | 6 (0.7) | 4 (0.5) | 4 (0.6) |
| 血中乳酸脱水素酵素増加 | 0 | 1 (0.1) | 0 |
| 血中リン減少 | 1 (0.1) | 1 (0.1) | 0 |
| 血中カリウム増加 | 2 (0.2) | 5 (0.6) | 2 (0.3) |
| 血圧上昇 | 5 (0.6) | 6 (0.7) | 5 (0.8) |
| 血中甲状腺刺激ホルモン減少 | 1 (0.1) | 0 | 0 |
| 血中トリグリセリド減少 | 0 | 0 | 1 (0.2) |
| 血中トリグリセリド増加 | 3 (0.4) | 1 (0.1) | 0 |
| 血中尿素増加 | 0 | 4 (0.5) | 1 (0.2) |
| 血中尿酸増加 | 4 (0.5) | 3 (0.4) | 0 |
| 心電図異常T波 | 1 (0.1) | 0 | 0 |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| 心電図T波逆転 | 0 | 1 (0.1) | 0 |
| γ－グルタミルトランスフェラーゼ異常 | 0 | 1 (0.1) | 0 |
| γ－グルタミルトランスフェラーゼ増加 | 0 | 2 (0.2) | 1 (0.2) |
| ヘマトクリット減少 | 0 | 0 | 1 (0.2) |
| ヘモグロビン減少 | 1 (0.1) | 5 (0.6) | 1 (0.2) |
| ヘリコバクター検査陽性 | 0 | 1 (0.1) | 0 |
| 肝酵素上昇 | 4 (0.5) | 7 (0.8) | 9 (1.4) |
| 高比重リポ蛋白増加 | 2 (0.2) | 1 (0.1) | 2 (0.3) |
| 眼圧上昇 | 0 | 1 (0.1) | 0 |
| 脂質増加 | 1 (0.1) | 0 | 0 |
| 肝機能検査値上昇 | 6 (0.7) | 6 (0.7) | 1 (0.2) |
| 低比重リポ蛋白減少 | 0 | 0 | 1 (0.2) |
| 低比重リポ蛋白増加 | 3 (0.4) | 2 (0.2) | 0 |
| リンパ球数減少 | 5 (0.6) | 8 (0.9) | 0 |
| 平均赤血球容積増加 | 6 (0.7) | 12 (1.4) | 1 (0.2) |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| 単球百分率減少 | 0 | 0 | 1 (0.2) |
| 筋酵素上昇 | 1 (0.1) | 0 | 0 |
| 骨髄球存在 | 1 (0.1) | 1 (0.1) | 0 |
| 好中球数減少 | 2 (0.2) | 14 (1.7) | 6 (1.0) |
| 好中球数増加 | 0 | 0 | 1 (0.2) |
| 好中球百分率増加 | 0 | 0 | 1 (0.2) |
| 核磁気共鳴画像異常 | 1 (0.1) | 0 | 0 |
| 便潜血陽性 | 1 (0.1) | 0 | 0 |
| 血小板数増加 | 1 (0.1) | 3 (0.4) | 1 (0.2) |
| 前立腺特異性抗原異常 | 1 (0.1) | 0 | 0 |
| 総蛋白増加 | 1 (0.1) | 0 | 0 |
| 尿中蛋白陽性 | 1 (0.1) | 0 | 1 (0.2) |
| 赤血球数減少 | 0 | 7 (0.8) | 3 (0.5) |
| 血沈亢進 | 1 (0.1) | 1 (0.1) | 0 |
| 血清フェリチン減少 | 0 | 1 (0.1) | 0 |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| ブドウ球菌検査陽性 | 0 | 1 (0.1) | 0 |
| レンサ球菌検査陽性 | 0 | 1 (0.1) | 0 |
| トランスアミナーゼ上昇 | 5 (0.6) | 11 (1.3) | 13 (2.1) |
| 超音波スキャン異常 | 0 | 0 | 1 (0.2) |
| 尿沈渣陽性 | 1 (0.1) | 0 | 0 |
| 尿検査異常 | 0 | 1 (0.1) | 1 (0.2) |
| 尿中白血球エステラーゼ陽性 | 0 | 1 (0.1) | 2 (0.3) |
| 尿量増加 | 0 | 0 | 1 (0.2) |
| 超低比重リポ蛋白増加 | 2 (0.2) | 4 (0.5) | 1 (0.2) |
| ビタミンB12減少 | 0 | 0 | 2 (0.3) |
| ビタミンD減少 | 0 | 0 | 1 (0.2) |
| 体重減少 | 3 (0.4) | 0 | 1 (0.2) |
| 体重増加 | 5 (0.6) | 5 (0.6) | 4 (0.6) |
| 白血球数減少 | 3 (0.4) | 18 (2.1) | 6 (1.0) |
| 白血球数増加 | 0 | 0 | 1 (0.2) |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| 尿中白血球陽性 | 0 | 0 | 1 (0.2) |
| 代謝および栄養障害 | 83 (9.9) | 88 (10.4) | 53 (8.4) |
| 炭水化物不耐症 | 1 (0.1) | 0 | 0 |
| 食欲減退 | 0 | 1 (0.1) | 1 (0.2) |
| 糖尿病 | 10 (1.2) | 5 (0.6) | 5 (0.8) |
| コントロール不良の糖尿病 | 1 (0.1) | 0 | 1 (0.2) |
| 脂質異常症 | 7 (0.8) | 15 (1.8) | 4 (0.6) |
| 体液貯留 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 耐糖能障害 | 4 (0.5) | 2 (0.2) | 4 (0.6) |
| グルテン過敏症 | 0 | 1 (0.1) | 0 |
| 痛風 | 1 (0.1) | 0 | 1 (0.2) |
| 高カルシウム血症 | 0 | 1 (0.1) | 0 |
| 高コレステロール血症 | 7 (0.8) | 15 (1.8) | 4 (0.6) |
| 高血糖 | 9 (1.1) | 10 (1.2) | 9 (1.4) |
| 高カリウム血症 | 1 (0.1) | 1 (0.1) | 0 |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 代謝および栄養障害 (Cont.) | | | |
| 高脂血症 | 5 (0.6) | 11 (1.3) | 1 (0.2) |
| 高トリグリセリド血症 | 1 (0.1) | 4 (0.5) | 6 (1.0) |
| 高尿酸血症 | 11 (1.3) | 9 (1.1) | 5 (0.8) |
| 低カルシウム血症 | 1 (0.1) | 0 | 0 |
| 低血糖 | 1 (0.1) | 0 | 1 (0.2) |
| 低カリウム血症 | 2 (0.2) | 0 | 1 (0.2) |
| 低ナトリウム血症 | 0 | 1 (0.1) | 0 |
| 低リン酸血症 | 1 (0.1) | 1 (0.1) | 0 |
| 空腹時血中ブドウ糖不良 | 0 | 2 (0.2) | 0 |
| 食欲亢進 | 1 (0.1) | 0 | 0 |
| インスリン抵抗性 | 2 (0.2) | 2 (0.2) | 0 |
| 鉄欠乏 | 1 (0.1) | 0 | 1 (0.2) |
| 代謝性アシドーシス | 0 | 0 | 1 (0.2) |
| 肥満 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 2型糖尿病 | 8 (1.0) | 2 (0.2) | 2 (0.3) |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 代謝および栄養障害 (Cont.) | | | |
| ビタミンB群欠乏 | 2 (0.2) | 0 | 0 |
| ビタミンB12欠乏 | 0 | 0 | 2 (0.3) |
| ビタミンD欠乏 | 4 (0.5) | 3 (0.4) | 2 (0.3) |
| 筋骨格系および結合組織障害 | 136 (16.2) | 167 (19.8) | 134 (21.2) |
| 後天性鉤爪趾 | 0 | 0 | 1 (0.2) |
| 関節痛 | 11 (1.3) | 13 (1.5) | 7 (1.1) |
| 関節炎 | 1 (0.1) | 0 | 1 (0.2) |
| 背部痛 | 11 (1.3) | 26 (3.1) | 20 (3.2) |
| 骨侵食 | 0 | 1 (0.1) | 0 |
| 骨腫脹 | 0 | 1 (0.1) | 0 |
| 滑液包炎 | 5 (0.6) | 6 (0.7) | 5 (0.8) |
| 頚部脊柱管狭窄症 | 1 (0.1) | 0 | 0 |
| 軟骨疾患 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 肋軟骨炎 | 1 (0.1) | 0 | 1 (0.2) |
| デュプイトラン拘縮 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 筋骨格系および結合組織障害 (Cont.) | | | |
| 線維筋痛 | 0 | 0 | 1 (0.2) |
| 側腹部痛 | 0 | 1 (0.1) | 0 |
| 足変形 | 1 (0.1) | 0 | 1 (0.2) |
| 椎間板線維輪断裂 | 0 | 1 (0.1) | 0 |
| 椎間板変性症 | 0 | 2 (0.2) | 0 |
| 椎間板障害 | 2 (0.2) | 1 (0.1) | 1 (0.2) |
| 椎間板突出 | 2 (0.2) | 4 (0.5) | 6 (1.0) |
| 関節過伸展 | 1 (0.1) | 0 | 0 |
| 関節不安定 | 0 | 0 | 1 (0.2) |
| 関節雑音 | 0 | 1 (0.1) | 0 |
| 関節硬直 | 1 (0.1) | 0 | 0 |
| 関節腫脹 | 1 (0.1) | 0 | 2 (0.3) |
| 腰部脊柱管狭窄症 | 1 (0.1) | 0 | 1 (0.2) |
| 咀嚼障害 | 0 | 0 | 1 (0.2) |
| 半月板変性 | 0 | 0 | 1 (0.2) |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 筋骨格系および結合組織障害 (Cont.) | | | |
| 中足骨痛 | 0 | 1 (0.1) | 0 |
| 筋拘縮 | 1 (0.1) | 0 | 0 |
| 筋肉疲労 | 1 (0.1) | 0 | 0 |
| 筋痙縮 | 7 (0.8) | 8 (0.9) | 7 (1.1) |
| 筋緊張 | 1 (0.1) | 0 | 0 |
| 筋力低下 | 1 (0.1) | 2 (0.2) | 0 |
| 筋骨格系胸痛 | 2 (0.2) | 5 (0.6) | 3 (0.5) |
| 筋骨格痛 | 4 (0.5) | 6 (0.7) | 2 (0.3) |
| 筋骨格硬直 | 0 | 1 (0.1) | 0 |
| 筋肉痛 | 3 (0.4) | 3 (0.4) | 2 (0.3) |
| 筋膜疼痛症候群 | 0 | 1 (0.1) | 0 |
| ミオパチー | 0 | 1 (0.1) | 0 |
| 筋炎 | 1 (0.1) | 0 | 0 |
| 頚部痛 | 1 (0.1) | 3 (0.4) | 2 (0.3) |
| 変形性関節症 | 11 (1.3) | 10 (1.2) | 8 (1.3) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 筋骨格系および結合組織障害 (Cont.) | | | |
| 骨端症 | 3 (0.4) | 0 | 1 (0.2) |
| 骨壊死 | 0 | 4 (0.5) | 0 |
| 骨減少症 | 2 (0.2) | 0 | 0 |
| 骨粗鬆症 | 3 (0.4) | 2 (0.2) | 1 (0.2) |
| 四肢痛 | 5 (0.6) | 4 (0.5) | 1 (0.2) |
| 顎痛 | 0 | 0 | 1 (0.2) |
| 病的骨折 | 1 (0.1) | 0 | 0 |
| 関節周囲炎 | 1 (0.1) | 2 (0.2) | 1 (0.2) |
| 足底筋膜炎 | 1 (0.1) | 4 (0.5) | 4 (0.6) |
| 乾癬性関節症 | 25 (3.0) | 34 (4.0) | 32 (5.1) |
| 肩回旋筋腱板症候群 | 4 (0.5) | 0 | 5 (0.8) |
| 仙腸骨炎 | 1 (0.1) | 0 | 0 |
| 側弯症 | 0 | 0 | 1 (0.2) |
| 軟部組織腫脹 | 1 (0.1) | 0 | 0 |
| 脊椎不安定 | 0 | 1 (0.1) | 0 |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 筋骨格系および結合組織障害 (Cont.) | | | |
| 変形性脊椎症 | 6 (0.7) | 5 (0.6) | 1 (0.2) |
| 脊椎痛 | 3 (0.4) | 2 (0.2) | 1 (0.2) |
| 脊椎後方すべり症 | 0 | 1 (0.1) | 0 |
| 脊柱管狭窄症 | 1 (0.1) | 0 | 1 (0.2) |
| 脊椎すべり症 | 0 | 0 | 2 (0.3) |
| 滑液嚢腫 | 3 (0.4) | 2 (0.2) | 0 |
| 滑膜炎 | 1 (0.1) | 0 | 1 (0.2) |
| 腱障害 | 0 | 1 (0.1) | 1 (0.2) |
| 腱痛 | 0 | 1 (0.1) | 0 |
| 腱炎 | 0 | 2 (0.2) | 0 |
| 腱鞘炎 | 1 (0.1) | 0 | 1 (0.2) |
| 狭窄性腱鞘炎 | 0 | 2 (0.2) | 1 (0.2) |
| 弾発指 | 1 (0.1) | 0 | 1 (0.2) |
| 椎間孔狭窄 | 0 | 1 (0.1) | 0 |
| 翼状肩甲骨 | 0 | 0 | 1 (0.2) |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 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) | 27 (3.2) | 22 (2.6) | 11 (1.7) |
| 結腸腺癌 | 0 | 1 (0.1) | 0 |
| 肛門性器疣贅 | 2 (0.2) | 1 (0.1) | 0 |
| 基底細胞癌 | 4 (0.5) | 2 (0.2) | 2 (0.3) |
| 肺の良性新生物 | 0 | 0 | 1 (0.2) |
| 副腎の良性新生物 | 0 | 1 (0.1) | 0 |
| 甲状腺の良性新生物 | 0 | 0 | 1 (0.2) |
| ボーエン病 | 0 | 1 (0.1) | 0 |
| 乳癌 | 0 | 1 (0.1) | 0 |
| 乳腺線維腫 | 1 (0.1) | 0 | 0 |
| 腎明細胞癌 | 0 | 1 (0.1) | 0 |
| 大腸腺腫 | 1 (0.1) | 1 (0.1) | 0 |
| 遠隔転移を伴う結腸癌 | 0 | 0 | 1 (0.2) |
| 子宮内膜腺癌 | 1 (0.1) | 0 | 0 |
| 肝臓血管腫 | 0 | 1 (0.1) | 1 (0.2) |

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E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 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)<br>(Cont.) | | | |
| 浸潤性乳癌 | 0 | 1 (0.1) | 0 |
| 脂肪腫 | 1 (0.1) | 0 | 0 |
| 乳房脂肪腫 | 1 (0.1) | 0 | 0 |
| 肺腺癌 | 1 (0.1) | 1 (0.1) | 0 |
| 遠隔転移を伴う肺癌 | 1 (0.1) | 0 | 0 |
| 悪性黒色腫 | 1 (0.1) | 0 | 0 |
| メラノサイト性母斑 | 1 (0.1) | 1 (0.1) | 0 |
| 単クローン性免疫グロブリン血症 | 0 | 1 (0.1) | 0 |
| 骨髄異形成症候群 | 1 (0.1) | 0 | 0 |
| 神経内分泌癌 | 1 (0.1) | 0 | 0 |
| 卵巣癌 | 0 | 0 | 1 (0.2) |
| 遠隔転移を伴う膵癌 | 0 | 0 | 1 (0.2) |
| 結膜乳頭腫 | 0 | 0 | 1 (0.2) |
| 形質細胞性骨髄腫 | 0 | 1 (0.1) | 0 |
| 脂漏性角化症 | 2 (0.2) | 0 | 1 (0.2) |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 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)<br>(Cont.) | | | |
| 皮膚乳頭腫 | 6 (0.7) | 4 (0.5) | 0 |
| 皮膚有棘細胞癌 | 2 (0.2) | 2 (0.2) | 0 |
| 子宮癌 | 0 | 0 | 1 (0.2) |
| 子宮平滑筋腫 | 0 | 1 (0.1) | 0 |
| 神経系障害 | 98 (11.7) | 99 (11.7) | 80 (12.7) |
| 異痛症 | 2 (0.2) | 0 | 0 |
| 意識変容状態 | 1 (0.1) | 0 | 0 |
| 健忘 | 0 | 1 (0.1) | 0 |
| 筋萎縮性側索硬化症 | 0 | 0 | 1 (0.2) |
| 灼熱感 | 1 (0.1) | 2 (0.2) | 1 (0.2) |
| 手根管症候群 | 3 (0.4) | 4 (0.5) | 3 (0.5) |
| 中枢性肺胞性低換気 | 1 (0.1) | 0 | 0 |
| 脳血管発作 | 0 | 0 | 2 (0.3) |
| 頚髄神経根障害 | 1 (0.1) | 2 (0.2) | 0 |
| 頚腕症候群 | 1 (0.1) | 0 | 0 |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 神経系障害 (Cont.) | | | |
| 認知障害 | 1 (0.1) | 0 | 0 |
| 頚頭蓋症候群 | 0 | 0 | 2 (0.3) |
| 認知症 | 0 | 0 | 1 (0.2) |
| 脱髄 | 0 | 1 (0.1) | 0 |
| 糖尿病性ニューロパチー | 0 | 1 (0.1) | 0 |
| 注意力障害 | 1 (0.1) | 0 | 0 |
| 浮動性めまい | 4 (0.5) | 7 (0.8) | 6 (1.0) |
| 体位性めまい | 0 | 1 (0.1) | 1 (0.2) |
| 異常感覚 | 0 | 0 | 1 (0.2) |
| 味覚異常 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 顔面麻痺 | 0 | 0 | 1 (0.2) |
| 蟻走感 | 1 (0.1) | 0 | 0 |
| 頭痛 | 43 (5.1) | 36 (4.3) | 29 (4.6) |
| 肝性脳症 | 0 | 0 | 1 (0.2) |
| 感覚鈍麻 | 3 (0.4) | 2 (0.2) | 3 (0.5) |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 神経系障害 (Cont.) | | | |
| 味覚減退 | 0 | 0 | 1 (0.2) |
| 肋間神経痛 | 1 (0.1) | 2 (0.2) | 0 |
| 虚血性ニューロパチー | 0 | 1 (0.1) | 0 |
| 虚血性脳卒中 | 1 (0.1) | 0 | 0 |
| ラクナ脳卒中 | 1 (0.1) | 0 | 0 |
| 嗜眠 | 1 (0.1) | 1 (0.1) | 0 |
| 腰髄神経根障害 | 2 (0.2) | 2 (0.2) | 2 (0.3) |
| 腰仙部神経根障害 | 0 | 1 (0.1) | 0 |
| 記憶障害 | 2 (0.2) | 2 (0.2) | 0 |
| 片頭痛 | 2 (0.2) | 5 (0.6) | 5 (0.8) |
| モートン神経痛 | 0 | 1 (0.1) | 0 |
| 神経痛 | 0 | 2 (0.2) | 0 |
| 末梢性ニューロパチー | 0 | 1 (0.1) | 0 |
| 錯感覚 | 2 (0.2) | 6 (0.7) | 2 (0.3) |
| 神経周囲嚢胞 | 0 | 0 | 1 (0.2) |

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Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 神経系障害 (Cont.) | | | |
| 末梢神経病変 | 1 (0.1) | 0 | 0 |
| 末梢性感覚ニューロパチー | 0 | 2 (0.2) | 0 |
| 睡眠の質低下 | 0 | 0 | 2 (0.3) |
| ヘルペス後神経痛 | 3 (0.4) | 4 (0.5) | 0 |
| 失神寸前の状態 | 0 | 1 (0.1) | 0 |
| 神経根痛 | 1 (0.1) | 1 (0.1) | 0 |
| 神経根障害 | 0 | 1 (0.1) | 1 (0.2) |
| 下肢静止不能症候群 | 0 | 0 | 1 (0.2) |
| 坐骨神経痛 | 8 (1.0) | 2 (0.2) | 5 (0.8) |
| 感覚障害 | 0 | 2 (0.2) | 0 |
| 副鼻腔炎に伴う頭痛 | 0 | 0 | 1 (0.2) |
| 傾眠 | 1 (0.1) | 1 (0.1) | 2 (0.3) |
| 失神 | 2 (0.2) | 0 | 1 (0.2) |
| 緊張性頭痛 | 3 (0.4) | 0 | 0 |
| 一過性脳虚血発作 | 0 | 1 (0.1) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 神経系障害 (Cont.) | | | |
| 振戦 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 三叉神経障害 | 1 (0.1) | 0 | 0 |
| 三叉神経痛 | 1 (0.1) | 0 | 1 (0.2) |
| 椎骨脳底動脈不全 | 0 | 1 (0.1) | 0 |
| 製品の問題 | 1 (0.1) | 2 (0.2) | 0 |
| 医療機器破損 | 1 (0.1) | 0 | 0 |
| 医療機器不具合 | 0 | 1 (0.1) | 0 |
| 医療機器材質の問題 | 0 | 1 (0.1) | 0 |
| 精神障害 | 40 (4.8) | 34 (4.0) | 14 (2.2) |
| 不安 | 6 (0.7) | 7 (0.8) | 4 (0.6) |
| 不安障害 | 3 (0.4) | 2 (0.2) | 0 |
| 双極性障害 | 1 (0.1) | 0 | 0 |
| 燃え尽き症候群 | 1 (0.1) | 0 | 0 |
| 抑うつ気分 | 2 (0.2) | 0 | 4 (0.6) |
| うつ病 | 7 (0.8) | 11 (1.3) | 3 (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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 精神障害 (Cont.) | | | |
| 摂食障害 | 0 | 1 (0.1) | 0 |
| 欲求不満耐性低下 | 0 | 1 (0.1) | 0 |
| 全般性不安障害 | 1 (0.1) | 0 | 0 |
| 不眠症 | 14 (1.7) | 10 (1.2) | 3 (0.5) |
| 混合性不安抑うつ障害 | 0 | 1 (0.1) | 0 |
| 神経過敏 | 1 (0.1) | 0 | 0 |
| 神経症 | 1 (0.1) | 0 | 0 |
| 睡眠障害 | 2 (0.2) | 1 (0.1) | 0 |
| ストレス | 1 (0.1) | 0 | 0 |
| 腎および尿路障害 | 46 (5.5) | 49 (5.8) | 30 (4.8) |
| 急性腎障害 | 0 | 2 (0.2) | 0 |
| 膀胱脱 | 1 (0.1) | 0 | 0 |
| 尿路結石 | 2 (0.2) | 1 (0.1) | 0 |
| 慢性腎臓病 | 2 (0.2) | 2 (0.2) | 0 |
| 結晶尿 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 腎および尿路障害 (Cont.) | | | |
| 腺性膀胱炎 | 1 (0.1) | 0 | 0 |
| 糖尿病性腎症 | 0 | 2 (0.2) | 0 |
| 排尿困難 | 4 (0.5) | 4 (0.5) | 3 (0.5) |
| 糖尿 | 0 | 1 (0.1) | 1 (0.2) |
| 血尿 | 9 (1.1) | 9 (1.1) | 4 (0.6) |
| 緊張性膀胱 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 腎うっ血 | 0 | 1 (0.1) | 0 |
| 白血球尿 | 4 (0.5) | 5 (0.6) | 0 |
| 尿意切迫 | 1 (0.1) | 0 | 0 |
| 腎結石症 | 5 (0.6) | 7 (0.8) | 6 (1.0) |
| 腎症 | 1 (0.1) | 0 | 0 |
| 頻尿 | 0 | 2 (0.2) | 0 |
| 多尿 | 0 | 0 | 1 (0.2) |
| 蛋白尿 | 6 (0.7) | 8 (0.9) | 5 (0.8) |
| 腎盂腎杯拡張症 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 腎および尿路障害 (Cont.) | | | |
| 腎仙痛 | 1 (0.1) | 0 | 3 (0.5) |
| 腎嚢胞 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 腎機能障害 | 2 (0.2) | 0 | 0 |
| 腎乳頭壊死 | 1 (0.1) | 0 | 0 |
| 腎静脈圧迫 | 0 | 1 (0.1) | 0 |
| 無菌性膿尿 | 0 | 0 | 1 (0.2) |
| 腹圧性尿失禁 | 0 | 0 | 1 (0.2) |
| 尿管結石症 | 2 (0.2) | 0 | 1 (0.2) |
| 尿失禁 | 1 (0.1) | 0 | 1 (0.2) |
| 尿閉 | 1 (0.1) | 0 | 0 |
| 尿路の炎症 | 0 | 0 | 1 (0.2) |
| 生殖系および乳房障害 | 41 (4.9) | 26 (3.1) | 12 (1.9) |
| 腺筋症 | 0 | 1 (0.1) | 0 |
| 無月経 | 1 (0.1) | 3 (0.4) | 1 (0.2) |
| 良性前立腺肥大症 | 1 (0.1) | 4 (0.5) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 生殖系および乳房障害 (Cont.) | | | |
| 乳房石灰化 | 1 (0.1) | 0 | 0 |
| 乳房嚢胞 | 3 (0.4) | 0 | 0 |
| 乳房障害 | 1 (0.1) | 0 | 0 |
| 乳房線維化 | 2 (0.2) | 0 | 0 |
| 乳房腫瘤 | 0 | 0 | 2 (0.3) |
| 前立腺結石 | 1 (0.1) | 0 | 0 |
| 子宮頚部嚢胞 | 0 | 1 (0.1) | 0 |
| 子宮頚部上皮異形成 | 1 (0.1) | 0 | 0 |
| 子宮頚管ポリープ | 0 | 1 (0.1) | 1 (0.2) |
| 膀胱瘤 | 1 (0.1) | 1 (0.1) | 0 |
| 月経困難症 | 0 | 0 | 1 (0.2) |
| 子宮頚外反 | 0 | 1 (0.1) | 0 |
| 子宮頚管内膜症 | 1 (0.1) | 0 | 0 |
| 子宮内膜増殖症 | 2 (0.2) | 0 | 0 |
| 子宮内膜症 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 生殖系および乳房障害 (Cont.) | | | |
| 精巣上体嚢胞 | 1 (0.1) | 0 | 0 |
| 勃起不全 | 0 | 1 (0.1) | 0 |
| 卵管嚢胞 | 1 (0.1) | 0 | 0 |
| 線維嚢胞性乳腺疾患 | 0 | 1 (0.1) | 0 |
| 女性化乳房 | 1 (0.1) | 0 | 0 |
| 出血性卵巣嚢胞 | 1 (0.1) | 0 | 0 |
| 閉経期症状 | 0 | 1 (0.1) | 0 |
| 月経過多 | 3 (0.4) | 0 | 0 |
| 不規則月経 | 5 (0.6) | 1 (0.1) | 0 |
| 不正子宮出血 | 1 (0.1) | 2 (0.2) | 0 |
| 卵巣嚢胞 | 2 (0.2) | 4 (0.5) | 1 (0.2) |
| 骨盤痛 | 1 (0.1) | 0 | 0 |
| 前立腺閉塞 | 1 (0.1) | 0 | 0 |
| 前立腺炎 | 3 (0.4) | 0 | 1 (0.2) |
| 前立腺腫大 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 生殖系および乳房障害 (Cont.) | | | |
| 直腸瘤 | 0 | 1 (0.1) | 0 |
| 陰嚢潰瘍 | 0 | 1 (0.1) | 0 |
| 精巣障害 | 1 (0.1) | 0 | 0 |
| 精巣腫脹 | 0 | 0 | 1 (0.2) |
| 子宮出血 | 1 (0.1) | 0 | 0 |
| 子宮ポリープ | 1 (0.1) | 0 | 0 |
| 子宮脱 | 2 (0.2) | 0 | 0 |
| 腟出血 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 腟脱 | 0 | 0 | 1 (0.2) |
| 呼吸器、胸郭および縦隔障害 | 81 (9.7) | 108 (12.8) | 64 (10.1) |
| アレルギー性咽頭炎 | 1 (0.1) | 0 | 0 |
| 喘息 | 2 (0.2) | 3 (0.4) | 2 (0.3) |
| 無気肺 | 0 | 1 (0.1) | 1 (0.2) |
| 慢性気管支炎 | 0 | 2 (0.2) | 0 |
| 気管支痙攣 | 3 (0.4) | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 呼吸器、胸郭および縦隔障害 (Cont.) | | | |
| カタル | 1 (0.1) | 0 | 1 (0.2) |
| 息詰まり | 0 | 0 | 1 (0.2) |
| 慢性閉塞性肺疾患 | 3 (0.4) | 4 (0.5) | 1 (0.2) |
| 咳嗽 | 23 (2.7) | 38 (4.5) | 11 (1.7) |
| 発声障害 | 1 (0.1) | 2 (0.2) | 0 |
| 呼吸困難 | 5 (0.6) | 10 (1.2) | 3 (0.5) |
| 労作性呼吸困難 | 1 (0.1) | 1 (0.1) | 0 |
| 鼻出血 | 5 (0.6) | 4 (0.5) | 2 (0.3) |
| 喀血 | 0 | 0 | 1 (0.2) |
| 間質性肺疾患 | 0 | 2 (0.2) | 0 |
| 下気道の炎症 | 0 | 0 | 1 (0.2) |
| 肺浸潤 | 0 | 0 | 1 (0.2) |
| 鼻閉 | 0 | 2 (0.2) | 3 (0.5) |
| 鼻部不快感 | 1 (0.1) | 0 | 0 |
| 鼻の炎症 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 呼吸器、胸郭および縦隔障害 (Cont.) | | | |
| 鼻閉塞 | 1 (0.1) | 0 | 0 |
| 鼻潰瘍 | 0 | 3 (0.4) | 0 |
| 口腔咽頭不快感 | 0 | 0 | 1 (0.2) |
| 口腔咽頭痛 | 12 (1.4) | 10 (1.2) | 12 (1.9) |
| 呼吸時疼痛 | 0 | 1 (0.1) | 0 |
| 咽頭の炎症 | 0 | 1 (0.1) | 1 (0.2) |
| 胸水 | 0 | 0 | 2 (0.3) |
| 胸膜炎 | 1 (0.1) | 0 | 0 |
| 肺臓炎 | 0 | 0 | 1 (0.2) |
| 自然気胸 | 0 | 1 (0.1) | 0 |
| 湿性咳嗽 | 0 | 0 | 1 (0.2) |
| 肺塞栓症 | 2 (0.2) | 3 (0.4) | 0 |
| 肺線維症 | 0 | 1 (0.1) | 1 (0.2) |
| 肺高血圧症 | 1 (0.1) | 0 | 0 |
| 肺腫瘤 | 0 | 3 (0.4) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 呼吸器、胸郭および縦隔障害 (Cont.) | | | |
| 呼吸窮迫 | 1 (0.1) | 0 | 0 |
| 気道うっ血 | 0 | 0 | 1 (0.2) |
| アレルギー性鼻炎 | 5 (0.6) | 3 (0.4) | 3 (0.5) |
| 鼻漏 | 5 (0.6) | 4 (0.5) | 3 (0.5) |
| 副鼻腔うっ血 | 0 | 1 (0.1) | 1 (0.2) |
| 副鼻腔障害 | 1 (0.1) | 0 | 0 |
| 睡眠時無呼吸症候群 | 2 (0.2) | 1 (0.1) | 1 (0.2) |
| 変色痰 | 1 (0.1) | 0 | 0 |
| 喀痰増加 | 1 (0.1) | 0 | 0 |
| 咽喉刺激感 | 0 | 3 (0.4) | 0 |
| 扁桃出血 | 0 | 0 | 2 (0.3) |
| 扁桃肥大 | 0 | 0 | 2 (0.3) |
| 扁桃の炎症 | 0 | 0 | 2 (0.3) |
| 上気道の炎症 | 2 (0.2) | 2 (0.2) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 皮膚および皮下組織障害 | 105 (12.5) | 124 (14.7) | 103 (16.3) |
| 黒色表皮腫 | 1 (0.1) | 0 | 0 |
| ざ瘡 | 6 (0.7) | 8 (0.9) | 0 |
| 光線性口唇炎 | 0 | 1 (0.1) | 0 |
| 光線角化症 | 2 (0.2) | 0 | 1 (0.2) |
| 脱毛症 | 4 (0.5) | 2 (0.2) | 9 (1.4) |
| 血管浮腫 | 2 (0.2) | 0 | 0 |
| 水疱 | 2 (0.2) | 4 (0.5) | 1 (0.2) |
| 肝斑 | 0 | 1 (0.1) | 0 |
| 慢性特発性蕁麻疹 | 1 (0.1) | 0 | 0 |
| 皮膚嚢腫 | 2 (0.2) | 2 (0.2) | 0 |
| 皮膚炎 | 3 (0.4) | 6 (0.7) | 4 (0.6) |
| ざ瘡様皮膚炎 | 0 | 3 (0.4) | 0 |
| アレルギー性皮膚炎 | 4 (0.5) | 6 (0.7) | 4 (0.6) |
| アトピー性皮膚炎 | 2 (0.2) | 0 | 0 |
| 接触皮膚炎 | 1 (0.1) | 2 (0.2) | 4 (0.6) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 皮膚および皮下組織障害 (Cont.) | | | |
| 薬疹 | 0 | 1 (0.1) | 1 (0.2) |
| 皮膚乾燥 | 1 (0.1) | 3 (0.4) | 1 (0.2) |
| 異汗性湿疹 | 1 (0.1) | 1 (0.1) | 0 |
| 湿疹 | 2 (0.2) | 2 (0.2) | 1 (0.2) |
| 紅斑 | 2 (0.2) | 6 (0.7) | 4 (0.6) |
| 環状紅斑 | 0 | 0 | 1 (0.2) |
| 毛髪成長異常 | 1 (0.1) | 0 | 0 |
| 多汗症 | 2 (0.2) | 1 (0.1) | 0 |
| 過角化 | 0 | 0 | 2 (0.3) |
| 嵌入爪 | 2 (0.2) | 0 | 4 (0.6) |
| 間擦疹 | 2 (0.2) | 1 (0.1) | 0 |
| 爪郭の炎症 | 0 | 1 (0.1) | 0 |
| 爪成長異常 | 1 (0.1) | 0 | 0 |
| 爪乾癬 | 1 (0.1) | 0 | 0 |
| 爪破損 | 1 (0.1) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 皮膚および皮下組織障害 (Cont.) | | | |
| 爪甲剥離症 | 0 | 1 (0.1) | 0 |
| 爪甲脱落症 | 3 (0.4) | 0 | 0 |
| 掌蹠膿疱症 | 1 (0.1) | 0 | 0 |
| 丘疹 | 0 | 1 (0.1) | 1 (0.2) |
| 口囲皮膚炎 | 1 (0.1) | 3 (0.4) | 1 (0.2) |
| 光線過敏性反応 | 0 | 0 | 1 (0.2) |
| そう痒症 | 1 (0.1) | 4 (0.5) | 11 (1.7) |
| 全身性そう痒症 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 乾癬 | 11 (1.3) | 24 (2.8) | 27 (4.3) |
| 紫斑 | 0 | 0 | 1 (0.2) |
| 膿疱性乾癬 | 0 | 1 (0.1) | 1 (0.2) |
| 発疹 | 5 (0.6) | 11 (1.3) | 5 (0.8) |
| 紅斑性皮疹 | 1 (0.1) | 2 (0.2) | 2 (0.3) |
| 毛孔性皮疹 | 1 (0.1) | 0 | 1 (0.2) |
| 全身性皮疹 | 1 (0.1) | 0 | 2 (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 study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 皮膚および皮下組織障害 (Cont.) | | | |
| 斑状皮疹 | 3 (0.4) | 2 (0.2) | 0 |
| 斑状丘疹状皮疹 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 丘疹性皮疹 | 3 (0.4) | 1 (0.1) | 0 |
| そう痒性皮疹 | 0 | 0 | 2 (0.3) |
| 酒さ | 8 (1.0) | 5 (0.6) | 0 |
| 痂皮 | 0 | 1 (0.1) | 0 |
| 脂漏性皮膚炎 | 0 | 3 (0.4) | 1 (0.2) |
| 皮膚変色 | 1 (0.1) | 0 | 0 |
| 皮膚障害 | 0 | 1 (0.1) | 0 |
| 皮膚剥脱 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 皮膚亀裂 | 0 | 1 (0.1) | 0 |
| 皮膚出血 | 1 (0.1) | 0 | 0 |
| 皮膚色素過剰 | 1 (0.1) | 0 | 0 |
| 皮膚色素減少 | 0 | 1 (0.1) | 0 |
| 皮膚刺激 | 1 (0.1) | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 皮膚および皮下組織障害 (Cont.) | | | |
| 皮膚病変 | 4 (0.5) | 2 (0.2) | 3 (0.5) |
| 顔面腫脹 | 1 (0.1) | 0 | 0 |
| 一過性棘融解性皮膚症 | 1 (0.1) | 0 | 0 |
| 蕁麻疹 | 7 (0.8) | 5 (0.6) | 4 (0.6) |
| 社会環境 | 4 (0.5) | 0 | 1 (0.2) |
| 閉経 | 3 (0.4) | 0 | 0 |
| 中年の転換期 | 0 | 0 | 1 (0.2) |
| 職場でのストレス | 1 (0.1) | 0 | 0 |
| 血管障害 | 58 (6.9) | 53 (6.3) | 31 (4.9) |
| 大動脈瘤 | 0 | 1 (0.1) | 1 (0.2) |
| 大動脈硬化症 | 0 | 1 (0.1) | 0 |
| 動脈狭窄 | 0 | 1 (0.1) | 0 |
| 動脈硬化症 | 0 | 1 (0.1) | 0 |
| 深部静脈血栓症 | 2 (0.2) | 1 (0.1) | 1 (0.2) |
| 血腫 | 1 (0.1) | 1 (0.1) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 血管障害 (Cont.) | | | |
| ほてり | 4 (0.5) | 1 (0.1) | 0 |
| 高血圧 | 47 (5.6) | 32 (3.8) | 17 (2.7) |
| 高血圧クリーゼ | 1 (0.1) | 0 | 1 (0.2) |
| 高血圧切迫症 | 0 | 1 (0.1) | 0 |
| 虚血 | 0 | 1 (0.1) | 0 |
| リンパ浮腫 | 0 | 1 (0.1) | 1 (0.2) |
| 起立性低血圧 | 0 | 3 (0.4) | 0 |
| 末梢冷感 | 0 | 0 | 2 (0.3) |
| 末梢静脈疾患 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| レイノー現象 | 0 | 0 | 3 (0.5) |
| 血栓性静脈炎 | 1 (0.1) | 0 | 1 (0.2) |
| 表在性血栓性静脈炎 | 0 | 3 (0.4) | 1 (0.2) |
| 静脈瘤 | 0 | 3 (0.4) | 0 |
| 血管炎 | 0 | 0 | 1 (0.2) |
| 血管拡張 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.2

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 血管障害 (Cont.) | | | |
| 静脈性高血圧 | 1 (0.1) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

表 2. 投与 56 週時カットオフまで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：M15-572 試験 CSR W56 Table 14.3__1.3

TABLE 14.3__1.3

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)

| | UPA | | |
|---|---|---|---|
| | 15 mg QD (N = 617) (PYs = 839.1) | 30 mg QD (N = 613) (PYs = 842.8) | ADA 40 mg EOW (N = 429) (PYs = 631.4) |
| System Organ Class<br>MedDRA 22.0 Preferred Term | Events (E/100 PYs) | Events (E/100 PYs) | Events (E/100 PYs) |
| Any adverse event | 969 (115.5) | 1242 (147.4) | 708 (112.1) |
| 血液およびリンパ系障害 | 78 (9.3) | 133 (15.8) | 39 (6.2) |
| 貧血 | 9 (1.1) | 17 (2.0) | 2 (0.3) |
| 大球性貧血 | 2 (0.2) | 4 (0.5) | 0 |
| 好塩基球増加症 | 0 | 1 (0.1) | 0 |
| 骨髄浮腫 | 0 | 1 (0.1) | 0 |
| 好酸球増加症 | 0 | 1 (0.1) | 0 |
| 赤血球減少症 | 0 | 3 (0.4) | 0 |
| 顆粒球減少症 | 0 | 3 (0.4) | 0 |
| 内出血発生の増加傾向 | 1 (0.1) | 1 (0.1) | 0 |
| 鉄欠乏性貧血 | 0 | 2 (0.2) | 1 (0.2) |
| 白血球増加症 | 0 | 3 (0.4) | 0 |
| 白血球減少症 | 24 (2.9) | 31 (3.7) | 10 (1.6) |
| リンパ節症 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| リンパ組織過形成 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 血液およびリンパ系障害 (Cont.) | | | |
| リンパ球減少症 | 22 (2.6) | 22 (2.6) | 1 (0.2) |
| 大赤血球症 | 0 | 0 | 1 (0.2) |
| 好中球減少症 | 15 (1.8) | 32 (3.8) | 18 (2.9) |
| 好中球増加症 | 2 (0.2) | 4 (0.5) | 1 (0.2) |
| 正色素性貧血 | 0 | 1 (0.1) | 0 |
| 正色素性正球性貧血 | 0 | 0 | 2 (0.3) |
| 血小板減少症 | 1 (0.1) | 1 (0.1) | 2 (0.3) |
| 血小板増加症 | 1 (0.1) | 4 (0.5) | 0 |
| 心臓障害 | 1 (0.1) | 5 (0.6) | 4 (0.6) |
| 狭心症 | 0 | 1 (0.1) | 0 |
| 心房細動 | 0 | 0 | 1 (0.2) |
| 房室ブロック | 0 | 1 (0.1) | 0 |
| 冠動脈疾患 | 0 | 0 | 1 (0.2) |
| 動悸 | 1 (0.1) | 0 | 0 |
| 洞性徐脈 | 0 | 1 (0.1) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 心臓障害 (Cont.) | | | |
| 頻脈 | 0 | 1 (0.1) | 0 |
| 発作性頻脈 | 0 | 1 (0.1) | 0 |
| 心室性期外収縮 | 0 | 0 | 1 (0.2) |
| 先天性、家族性および遺伝性障害 | 1 (0.1) | 0 | 0 |
| 陰嚢水瘤 | 1 (0.1) | 0 | 0 |
| 耳および迷路障害 | 1 (0.1) | 1 (0.1) | 2 (0.3) |
| 耳鳴 | 0 | 0 | 1 (0.2) |
| 回転性めまい | 0 | 0 | 1 (0.2) |
| 頭位性回転性めまい | 1 (0.1) | 1 (0.1) | 0 |
| 内分泌障害 | 1 (0.1) | 0 | 0 |
| アンドロゲン欠乏症 | 1 (0.1) | 0 | 0 |
| 眼障害 | 5 (0.6) | 3 (0.4) | 2 (0.3) |
| 眼瞼痙攣 | 1 (0.1) | 0 | 0 |
| ドライアイ | 0 | 1 (0.1) | 0 |
| 眼痛 | 1 (0.1) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 眼障害 (Cont.) | | | |
| 虹彩毛様体炎 | 0 | 1 (0.1) | 0 |
| 角膜炎 | 0 | 0 | 1 (0.2) |
| 瞼板腺炎 | 1 (0.1) | 0 | 1 (0.2) |
| 眼部不快感 | 0 | 1 (0.1) | 0 |
| 霧視 | 1 (0.1) | 0 | 0 |
| 視力障害 | 1 (0.1) | 0 | 0 |
| 胃腸障害 | 67 (8.0) | 65 (7.7) | 48 (7.6) |
| 腹部不快感 | 1 (0.1) | 2 (0.2) | 0 |
| 腹部膨満 | 0 | 2 (0.2) | 0 |
| 腹痛 | 4 (0.5) | 1 (0.1) | 1 (0.2) |
| 上腹部痛 | 5 (0.6) | 8 (0.9) | 3 (0.5) |
| 口角口唇炎 | 1 (0.1) | 1 (0.1) | 0 |
| アフタ性潰瘍 | 2 (0.2) | 1 (0.1) | 1 (0.2) |
| 根尖肉芽腫 | 0 | 1 (0.1) | 0 |
| 便秘 | 3 (0.4) | 3 (0.4) | 4 (0.6) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 下痢 | 12 (1.4) | 11 (1.3) | 8 (1.3) |
| 憩室 | 1 (0.1) | 0 | 1 (0.2) |
| 口内乾燥 | 0 | 1 (0.1) | 1 (0.2) |
| 十二指腸潰瘍 | 0 | 0 | 1 (0.2) |
| 消化不良 | 2 (0.2) | 2 (0.2) | 1 (0.2) |
| 小腸炎 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 腸炎 | 0 | 1 (0.1) | 0 |
| びらん性十二指腸炎 | 1 (0.1) | 0 | 0 |
| 鼓腸 | 1 (0.1) | 3 (0.4) | 0 |
| 食中毒 | 1 (0.1) | 0 | 0 |
| 胃炎 | 2 (0.2) | 3 (0.4) | 1 (0.2) |
| びらん性胃炎 | 2 (0.2) | 0 | 0 |
| 胃十二指腸出血 | 1 (0.1) | 0 | 0 |
| 胃十二指腸潰瘍 | 0 | 1 (0.1) | 0 |
| 胃食道逆流性疾患 | 3 (0.4) | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 歯肉退縮 | 0 | 0 | 1 (0.2) |
| 舌炎 | 1 (0.1) | 0 | 0 |
| 血便排泄 | 1 (0.1) | 0 | 0 |
| 痔核 | 1 (0.1) | 0 | 0 |
| 裂孔ヘルニア | 0 | 0 | 1 (0.2) |
| 腸管ポリープ | 0 | 0 | 1 (0.2) |
| 口腔内白斑症 | 0 | 0 | 1 (0.2) |
| メレナ | 0 | 0 | 1 (0.2) |
| 口腔内潰瘍形成 | 2 (0.2) | 4 (0.5) | 1 (0.2) |
| 悪心 | 9 (1.1) | 8 (0.9) | 10 (1.6) |
| 食道潰瘍 | 0 | 1 (0.1) | 0 |
| 食道炎 | 0 | 0 | 1 (0.2) |
| 口腔粘膜水疱形成 | 0 | 1 (0.1) | 0 |
| 膵炎 | 1 (0.1) | 0 | 0 |
| 歯周の炎症 | 1 (0.1) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| レッチング | 1 (0.1) | 0 | 0 |
| 流涎過多 | 0 | 0 | 1 (0.2) |
| 口内炎 | 3 (0.4) | 3 (0.4) | 1 (0.2) |
| 舌障害 | 0 | 0 | 1 (0.2) |
| 舌潰瘍 | 1 (0.1) | 1 (0.1) | 0 |
| 歯の障害 | 1 (0.1) | 0 | 0 |
| 歯痛 | 1 (0.1) | 0 | 0 |
| 上部消化管出血 | 0 | 1 (0.1) | 0 |
| 嘔吐 | 1 (0.1) | 3 (0.4) | 5 (0.8) |
| 一般・全身障害および投与部位の状態 | 16 (1.9) | 27 (3.2) | 53 (8.4) |
| 医薬品副作用 | 0 | 0 | 1 (0.2) |
| 無力症 | 1 (0.1) | 3 (0.4) | 0 |
| 悪寒 | 1 (0.1) | 1 (0.1) | 0 |
| 疲労 | 5 (0.6) | 4 (0.5) | 3 (0.5) |
| 炎症 | 0 | 1 (0.1) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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)

| | UPA | | |
|---|---|---|---|
| | 15 mg QD (N = 617) (PYs = 839.1) | 30 mg QD (N = 613) (PYs = 842.8) | ADA 40 mg EOW (N = 429) (PYs = 631.4) |
| System Organ Class<br>MedDRA 22.0 Preferred Term | Events (E/100 PYs) | Events (E/100 PYs) | Events (E/100 PYs) |
| 一般・全身障害および投与部位の状態 (Cont.) | | | |
| インフルエンザ様疾患 | 0 | 3 (0.4) | 1 (0.2) |
| 注射部位内出血 | 0 | 0 | 3 (0.5) |
| 注射部位湿疹 | 0 | 0 | 3 (0.5) |
| 注射部位紅斑 | 0 | 0 | 5 (0.8) |
| 注射部位過敏反応 | 0 | 0 | 1 (0.2) |
| 注射部位硬結 | 0 | 0 | 1 (0.2) |
| 注射部位疼痛 | 0 | 1 (0.1) | 4 (0.6) |
| 注射部位そう痒感 | 0 | 0 | 2 (0.3) |
| 注射部位反応 | 0 | 1 (0.1) | 20 (3.2) |
| 注射部位蕁麻疹 | 0 | 0 | 3 (0.5) |
| 倦怠感 | 2 (0.2) | 0 | 1 (0.2) |
| 疼痛 | 0 | 1 (0.1) | 2 (0.3) |
| 末梢腫脹 | 1 (0.1) | 1 (0.1) | 0 |
| 発熱 | 6 (0.7) | 10 (1.2) | 2 (0.3) |
| 腫脹 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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)

| | UPA | | |
|---|---|---|---|
| System Organ Class<br>MedDRA 22.0 Preferred Term | 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
| 肝胆道系障害 | 15 (1.8) | 19 (2.3) | 9 (1.4) |
| 慢性胆嚢炎 | 0 | 1 (0.1) | 0 |
| 胆石症 | 0 | 0 | 1 (0.2) |
| 肝機能異常 | 9 (1.1) | 10 (1.2) | 2 (0.3) |
| 肝腫瘤 | 0 | 1 (0.1) | 0 |
| 脂肪肝 | 1 (0.1) | 3 (0.4) | 0 |
| 肝炎 | 1 (0.1) | 1 (0.1) | 0 |
| 肝毒性 | 1 (0.1) | 1 (0.1) | 0 |
| 高ビリルビン血症 | 1 (0.1) | 1 (0.1) | 0 |
| 高トランスアミナーゼ血症 | 0 | 0 | 1 (0.2) |
| 黄疸 | 0 | 0 | 1 (0.2) |
| 肝障害 | 0 | 1 (0.1) | 2 (0.3) |
| 肝損傷 | 0 | 0 | 1 (0.2) |
| 非アルコール性脂肪性肝炎 | 1 (0.1) | 0 | 0 |
| 門脈血栓症 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 肝胆道系障害 (Cont.) | | | |
| 脂肪性肝炎 | 1 (0.1) | 0 | 0 |
| 免疫系障害 | 0 | 3 (0.4) | 3 (0.5) |
| 食物アレルギー | 0 | 1 (0.1) | 0 |
| 過敏症 | 0 | 1 (0.1) | 3 (0.5) |
| 免疫系障害 | 0 | 1 (0.1) | 0 |
| 感染症および寄生虫症 | 379 (45.2) | 463 (54.9) | 229 (36.3) |
| 腹部膿瘍 | 0 | 1 (0.1) | 0 |
| 腹壁膿瘍 | 1 (0.1) | 0 | 0 |
| 四肢膿瘍 | 0 | 4 (0.5) | 1 (0.2) |
| 急性副鼻腔炎 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 歯槽骨炎 | 0 | 0 | 1 (0.2) |
| 虫垂炎 | 0 | 1 (0.1) | 0 |
| 異型肺炎 | 0 | 1 (0.1) | 0 |
| 菌血症 | 0 | 1 (0.1) | 0 |
| 細菌感染 | 1 (0.1) | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 体部白癬 | 1 (0.1) | 0 | 0 |
| 骨髄炎 | 0 | 0 | 1 (0.2) |
| 気管支炎 | 22 (2.6) | 27 (3.2) | 7 (1.1) |
| 細菌性気管支炎 | 1 (0.1) | 1 (0.1) | 0 |
| 蜂巣炎 | 3 (0.4) | 3 (0.4) | 10 (1.6) |
| 慢性扁桃炎 | 0 | 0 | 1 (0.2) |
| 結膜炎 | 2 (0.2) | 0 | 3 (0.5) |
| ウイルス性結膜炎 | 1 (0.1) | 0 | 0 |
| コロナウイルス感染 | 0 | 3 (0.4) | 0 |
| 膀胱炎 | 3 (0.4) | 3 (0.4) | 4 (0.6) |
| サイトメガロウイルス感染 | 0 | 1 (0.1) | 0 |
| 毛嚢虫症 | 1 (0.1) | 0 | 0 |
| 憩室炎 | 2 (0.2) | 0 | 1 (0.2) |
| 耳感染 | 4 (0.5) | 1 (0.1) | 1 (0.2) |
| 丹毒 | 2 (0.2) | 1 (0.1) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 大腸菌性尿路感染 | 2 (0.2) | 3 (0.4) | 0 |
| 眼感染 | 0 | 0 | 2 (0.3) |
| 熱性感染症 | 1 (0.1) | 0 | 0 |
| 毛包炎 | 10 (1.2) | 5 (0.6) | 1 (0.2) |
| 真菌感染 | 1 (0.1) | 0 | 0 |
| 皮膚真菌感染 | 3 (0.4) | 8 (0.9) | 3 (0.5) |
| せつ | 3 (0.4) | 0 | 0 |
| 胃腸炎 | 10 (1.2) | 10 (1.2) | 3 (0.5) |
| ウイルス性胃腸炎 | 0 | 4 (0.5) | 0 |
| 消化管感染 | 1 (0.1) | 0 | 0 |
| 陰部ヘルペス | 2 (0.2) | 1 (0.1) | 0 |
| 陰部単純ヘルペス | 1 (0.1) | 0 | 1 (0.2) |
| 歯肉炎 | 1 (0.1) | 3 (0.4) | 0 |
| 肛径部膿瘍 | 0 | 1 (0.1) | 0 |
| H1N1インフルエンザ | 2 (0.2) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| B型肝炎 | 0 | 1 (0.1) | 0 |
| B型肝炎再活性化 | 1 (0.1) | 0 | 0 |
| ヘルペス眼感染 | 0 | 1 (0.1) | 0 |
| 単純ヘルペス | 3 (0.4) | 12 (1.4) | 1 (0.2) |
| ヘルペスウイルス感染 | 1 (0.1) | 0 | 0 |
| 帯状疱疹 | 27 (3.2) | 40 (4.7) | 3 (0.5) |
| 皮膚播種性帯状疱疹 | 0 | 1 (0.1) | 0 |
| 麦粒腫 | 1 (0.1) | 0 | 0 |
| 伝染性単核症 | 0 | 1 (0.1) | 0 |
| インフルエンザ | 15 (1.8) | 14 (1.7) | 2 (0.3) |
| 注射部位感染 | 1 (0.1) | 0 | 0 |
| クレブシエラ感染 | 1 (0.1) | 0 | 0 |
| 喉頭炎 | 0 | 4 (0.5) | 1 (0.2) |
| 潜伏結核 | 9 (1.1) | 3 (0.4) | 4 (0.6) |
| 限局性感染 | 1 (0.1) | 1 (0.1) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 下気道感染 | 3 (0.4) | 3 (0.4) | 3 (0.5) |
| 肺感染 | 0 | 3 (0.4) | 0 |
| リンパ管炎 | 0 | 1 (0.1) | 0 |
| ムンプス | 1 (0.1) | 0 | 0 |
| 爪感染 | 0 | 4 (0.5) | 0 |
| 鼻ヘルペス | 0 | 0 | 2 (0.3) |
| 上咽頭炎 | 26 (3.1) | 23 (2.7) | 36 (5.7) |
| 爪真菌症 | 1 (0.1) | 1 (0.1) | 2 (0.3) |
| 口腔カンジダ症 | 2 (0.2) | 4 (0.5) | 1 (0.2) |
| 口腔真菌感染 | 1 (0.1) | 1 (0.1) | 0 |
| 口腔ヘルペス | 13 (1.5) | 46 (5.5) | 12 (1.9) |
| 中咽頭カンジダ症 | 0 | 1 (0.1) | 0 |
| 外耳炎 | 0 | 2 (0.2) | 0 |
| 中耳炎 | 0 | 1 (0.1) | 2 (0.3) |
| 急性中耳炎 | 0 | 3 (0.4) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 爪囲炎 | 3 (0.4) | 3 (0.4) | 1 (0.2) |
| 歯周炎 | 2 (0.2) | 1 (0.1) | 0 |
| 咽頭炎 | 7 (0.8) | 4 (0.5) | 3 (0.5) |
| 細菌性咽頭炎 | 1 (0.1) | 0 | 0 |
| レンサ球菌性咽頭炎 | 1 (0.1) | 0 | 1 (0.2) |
| ニューモシスチス・イロベチイ肺炎 | 0 | 1 (0.1) | 0 |
| 肺炎 | 4 (0.5) | 5 (0.6) | 4 (0.6) |
| 細菌性肺炎 | 1 (0.1) | 0 | 0 |
| レンサ球菌性肺炎 | 0 | 1 (0.1) | 0 |
| 歯髄炎 | 2 (0.2) | 0 | 0 |
| 化膿性分泌物 | 0 | 1 (0.1) | 0 |
| 腎盂腎炎 | 0 | 1 (0.1) | 0 |
| 急性腎盂腎炎 | 0 | 2 (0.2) | 0 |
| 膿疱性皮疹 | 0 | 4 (0.5) | 0 |
| 気道感染 | 15 (1.8) | 10 (1.2) | 3 (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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| ウイルス性気道感染 | 1 (0.1) | 2 (0.2) | 0 |
| 鼻炎 | 0 | 5 (0.6) | 4 (0.6) |
| サルモネラ症 | 0 | 0 | 1 (0.2) |
| 卵管炎 | 0 | 1 (0.1) | 0 |
| 敗血症 | 2 (0.2) | 0 | 0 |
| 副鼻腔炎 | 6 (0.7) | 13 (1.5) | 9 (1.4) |
| 皮膚感染 | 2 (0.2) | 1 (0.1) | 0 |
| 軟部組織感染 | 0 | 0 | 2 (0.3) |
| ブドウ球菌性菌血症 | 0 | 1 (0.1) | 0 |
| ブドウ球菌感染 | 1 (0.1) | 0 | 1 (0.2) |
| ブドウ球菌性敗血症 | 0 | 1 (0.1) | 0 |
| ブドウ球菌皮膚感染 | 1 (0.1) | 0 | 0 |
| 皮下組織膿瘍 | 0 | 1 (0.1) | 0 |
| 白癬感染 | 1 (0.1) | 0 | 1 (0.2) |
| 手白癬 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 足部白癬 | 4 (0.5) | 1 (0.1) | 1 (0.2) |
| 癜風 | 2 (0.2) | 0 | 1 (0.2) |
| 扁桃炎 | 4 (0.5) | 4 (0.5) | 2 (0.3) |
| 細菌性扁桃炎 | 5 (0.6) | 1 (0.1) | 0 |
| 歯膿瘍 | 3 (0.4) | 0 | 0 |
| 歯感染 | 2 (0.2) | 4 (0.5) | 0 |
| 気管炎 | 1 (0.1) | 3 (0.4) | 0 |
| 気管気管支炎 | 2 (0.2) | 3 (0.4) | 0 |
| トリコモナス症 | 0 | 0 | 1 (0.2) |
| トリコフィトン感染症 | 1 (0.1) | 0 | 0 |
| 上気道感染 | 73 (8.7) | 83 (9.8) | 52 (8.2) |
| 尿路感染 | 30 (3.6) | 32 (3.8) | 14 (2.2) |
| 細菌性尿路感染 | 0 | 1 (0.1) | 0 |
| 尿路性敗血症 | 0 | 1 (0.1) | 0 |
| 膣感染 | 0 | 0 | 2 (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 study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| ウイルス感染 | 0 | 3 (0.4) | 1 (0.2) |
| ウイルス性咽頭炎 | 1 (0.1) | 1 (0.1) | 0 |
| ウイルス性副鼻腔炎 | 0 | 1 (0.1) | 0 |
| ウイルス性気管炎 | 2 (0.2) | 0 | 0 |
| ウイルス性上気道感染 | 4 (0.5) | 1 (0.1) | 5 (0.8) |
| 外陰部膿瘍 | 0 | 0 | 2 (0.3) |
| 女性外陰部蜂巣炎 | 0 | 0 | 1 (0.2) |
| 外陰部炎 | 1 (0.1) | 0 | 0 |
| 外陰部腟カンジダ症 | 3 (0.4) | 3 (0.4) | 1 (0.2) |
| 外陰腟真菌感染 | 2 (0.2) | 6 (0.7) | 1 (0.2) |
| 外陰腟炎 | 0 | 1 (0.1) | 0 |
| 創傷感染 | 0 | 0 | 1 (0.2) |
| 傷害、中毒および処置合併症 | 1 (0.1) | 5 (0.6) | 3 (0.5) |
| 偶発的過量投与 | 0 | 0 | 1 (0.2) |
| 節足動物咬傷 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 傷害、中毒および処置合併症 (Cont.) | | | |
| 挫傷 | 0 | 1 (0.1) | 1 (0.2) |
| 大腿骨骨折 | 0 | 1 (0.1) | 0 |
| 仙骨骨折 | 0 | 1 (0.1) | 0 |
| 注射に伴う反応 | 0 | 0 | 1 (0.2) |
| 処置による疼痛 | 0 | 1 (0.1) | 0 |
| 皮膚擦過傷 | 1 (0.1) | 0 | 0 |
| 臨床検査 | 235 (28.0) | 305 (36.2) | 171 (27.1) |
| アラニンアミノトランスフェラーゼ異常 | 0 | 1 (0.1) | 0 |
| アラニンアミノトランスフェラーゼ増加 | 57 (6.8) | 45 (5.3) | 42 (6.7) |
| αヒドロキシ酪酸脱水素酵素増加 | 0 | 1 (0.1) | 0 |
| アスパラギン酸アミノトランスフェラーゼ異常 | 0 | 1 (0.1) | 0 |
| アスパラギン酸アミノトランスフェラーゼ増加 | 39 (4.6) | 37 (4.4) | 31 (4.9) |
| 血中アルカリホスファターゼ増加 | 1 (0.1) | 0 | 0 |
| 血中ビリルビン増加 | 2 (0.2) | 2 (0.2) | 6 (1.0) |
| 血中コレステロール増加 | 5 (0.6) | 4 (0.5) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| 血中クレアチンホスホキナーゼ増加 | 77 (9.2) | 109 (12.9) | 33 (5.2) |
| 血中クレアチニン増加 | 4 (0.5) | 5 (0.6) | 2 (0.3) |
| 血中ブドウ糖異常 | 1 (0.1) | 0 | 0 |
| 血中ブドウ糖増加 | 1 (0.1) | 0 | 2 (0.3) |
| 血中乳酸脱水素酵素増加 | 0 | 1 (0.1) | 0 |
| 血中リン減少 | 1 (0.1) | 0 | 0 |
| 血中カリウム増加 | 0 | 5 (0.6) | 1 (0.2) |
| 血圧上昇 | 2 (0.2) | 3 (0.4) | 4 (0.6) |
| 血中甲状腺刺激ホルモン減少 | 1 (0.1) | 0 | 0 |
| 血中トリグリセリド減少 | 0 | 0 | 1 (0.2) |
| 血中トリグリセリド増加 | 1 (0.1) | 1 (0.1) | 0 |
| 血中尿素増加 | 0 | 1 (0.1) | 0 |
| 血中尿酸増加 | 1 (0.1) | 3 (0.4) | 0 |
| 心電図異常T波 | 1 (0.1) | 0 | 0 |
| γ－グルタミルトランスフェラーゼ異常 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| γ－グルタミルトランスフェラーゼ増加 | 0 | 0 | 1 (0.2) |
| ヘマトクリット減少 | 0 | 0 | 1 (0.2) |
| ヘモグロビン減少 | 1 (0.1) | 3 (0.4) | 0 |
| 肝酵素上昇 | 3 (0.4) | 3 (0.4) | 6 (1.0) |
| 高比重リポ蛋白増加 | 2 (0.2) | 1 (0.1) | 2 (0.3) |
| 肝機能検査値上昇 | 4 (0.5) | 2 (0.2) | 1 (0.2) |
| 低比重リポ蛋白減少 | 0 | 0 | 1 (0.2) |
| 低比重リポ蛋白増加 | 3 (0.4) | 2 (0.2) | 0 |
| リンパ球数減少 | 5 (0.6) | 7 (0.8) | 0 |
| 平均赤血球容積増加 | 6 (0.7) | 8 (0.9) | 1 (0.2) |
| 単球百分率減少 | 0 | 0 | 1 (0.2) |
| 筋酵素上昇 | 1 (0.1) | 0 | 0 |
| 骨髄球存在 | 1 (0.1) | 1 (0.1) | 0 |
| 好中球数減少 | 2 (0.2) | 14 (1.7) | 5 (0.8) |
| 血小板数増加 | 1 (0.1) | 3 (0.4) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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)

| | UPA | | |
|---|---|---|---|
| | 15 mg QD (N = 617) (PYs = 839.1) | 30 mg QD (N = 613) (PYs = 842.8) | ADA 40 mg EOW (N = 429) (PYs = 631.4) |
| System Organ Class<br>MedDRA 22.0 Preferred Term | Events (E/100 PYs) | Events (E/100 PYs) | Events (E/100 PYs) |
| 臨床検査 (Cont.) | | | |
| 総蛋白増加 | 1 (0.1) | 0 | 0 |
| 尿中蛋白陽性 | 0 | 0 | 1 (0.2) |
| 赤血球数減少 | 0 | 7 (0.8) | 2 (0.3) |
| 血沈亢進 | 1 (0.1) | 0 | 0 |
| ブドウ球菌検査陽性 | 0 | 1 (0.1) | 0 |
| レンサ球菌検査陽性 | 0 | 1 (0.1) | 0 |
| トランスアミナーゼ上昇 | 2 (0.2) | 7 (0.8) | 10 (1.6) |
| 尿検査異常 | 0 | 1 (0.1) | 1 (0.2) |
| 尿中白血球エステラーゼ陽性 | 0 | 0 | 2 (0.3) |
| 尿量増加 | 0 | 0 | 1 (0.2) |
| 超低比重リポ蛋白増加 | 2 (0.2) | 4 (0.5) | 1 (0.2) |
| 体重減少 | 0 | 0 | 1 (0.2) |
| 体重増加 | 3 (0.4) | 2 (0.2) | 2 (0.3) |
| 白血球数減少 | 3 (0.4) | 18 (2.1) | 6 (1.0) |
| 尿中白血球陽性 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 代謝および栄養障害 | 21 (2.5) | 33 (3.9) | 19 (3.0) |
| 糖尿病 | 0 | 0 | 1 (0.2) |
| コントロール不良の糖尿病 | 0 | 0 | 1 (0.2) |
| 脂質異常症 | 3 (0.4) | 8 (0.9) | 3 (0.5) |
| 耐糖能障害 | 0 | 0 | 1 (0.2) |
| 高カルシウム血症 | 0 | 1 (0.1) | 0 |
| 高コレステロール血症 | 3 (0.4) | 8 (0.9) | 1 (0.2) |
| 高血糖 | 1 (0.1) | 3 (0.4) | 4 (0.6) |
| 高脂血症 | 4 (0.5) | 8 (0.9) | 1 (0.2) |
| 高トリグリセリド血症 | 0 | 0 | 3 (0.5) |
| 高尿酸血症 | 7 (0.8) | 3 (0.4) | 3 (0.5) |
| 低血糖 | 1 (0.1) | 0 | 0 |
| 低カリウム血症 | 1 (0.1) | 0 | 1 (0.2) |
| 低リン酸血症 | 1 (0.1) | 1 (0.1) | 0 |
| ビタミンD欠乏 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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)

| | UPA | | |
|---|---|---|---|
| System Organ Class<br>MedDRA 22.0 Preferred Term | 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
| 筋骨格系および結合組織障害 | 15 (1.8) | 15 (1.8) | 14 (2.2) |
| 関節痛 | 0 | 0 | 1 (0.2) |
| 関節炎 | 1 (0.1) | 0 | 0 |
| 背部痛 | 0 | 0 | 2 (0.3) |
| 軟骨疾患 | 0 | 1 (0.1) | 0 |
| 側腹部痛 | 0 | 1 (0.1) | 0 |
| 関節雑音 | 0 | 1 (0.1) | 0 |
| 関節硬直 | 1 (0.1) | 0 | 0 |
| 筋痙縮 | 2 (0.2) | 1 (0.1) | 2 (0.3) |
| 筋力低下 | 1 (0.1) | 1 (0.1) | 0 |
| 筋骨格系胸痛 | 0 | 3 (0.4) | 0 |
| 筋肉痛 | 2 (0.2) | 2 (0.2) | 0 |
| ミオパチー | 0 | 1 (0.1) | 0 |
| 頚部痛 | 0 | 0 | 1 (0.2) |
| 骨端症 | 1 (0.1) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 筋骨格系および結合組織障害 (Cont.) | | | |
| 骨粗鬆症 | 0 | 1 (0.1) | 0 |
| 四肢痛 | 1 (0.1) | 0 | 1 (0.2) |
| 関節周囲炎 | 0 | 1 (0.1) | 0 |
| 乾癬性関節症 | 5 (0.6) | 2 (0.2) | 6 (1.0) |
| 脊椎痛 | 1 (0.1) | 0 | 1 (0.2) |
| 良性、悪性および詳細不明の新生物(嚢胞およびポリープを含む) | 9 (1.1) | 13 (1.5) | 2 (0.3) |
| 結腸腺癌 | 0 | 1 (0.1) | 0 |
| 肛門性器疣贅 | 0 | 1 (0.1) | 0 |
| 基底細胞癌 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| ボーエン病 | 0 | 1 (0.1) | 0 |
| 乳癌 | 0 | 1 (0.1) | 0 |
| 肺腺癌 | 1 (0.1) | 0 | 0 |
| 遠隔転移を伴う肺癌 | 1 (0.1) | 0 | 0 |
| メラノサイト性母斑 | 0 | 1 (0.1) | 0 |
| 遠隔転移を伴う膵癌 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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)

| | UPA | | |
|---|---|---|---|
| | 15 mg QD (N = 617) (PYs = 839.1) | 30 mg QD (N = 613) (PYs = 842.8) | ADA 40 mg EOW (N = 429) (PYs = 631.4) |
| System Organ Class<br>MedDRA 22.0 Preferred Term | Events (E/100 PYs) | Events (E/100 PYs) | Events (E/100 PYs) |
| 良性、悪性および詳細不明の新生物(嚢胞およびポリープを含む) (Cont.) | | | |
| 形質細胞性骨髄腫 | 0 | 1 (0.1) | 0 |
| 脂漏性角化症 | 1 (0.1) | 0 | 0 |
| 皮膚乳頭腫 | 3 (0.4) | 4 (0.5) | 0 |
| 皮膚有棘細胞癌 | 2 (0.2) | 2 (0.2) | 0 |
| 神経系障害 | 24 (2.9) | 32 (3.8) | 16 (2.5) |
| 灼熱感 | 0 | 2 (0.2) | 0 |
| 手根管症候群 | 0 | 1 (0.1) | 0 |
| 浮動性めまい | 3 (0.4) | 2 (0.2) | 1 (0.2) |
| 体位性めまい | 0 | 0 | 1 (0.2) |
| 頭痛 | 14 (1.7) | 12 (1.4) | 8 (1.3) |
| 肝性脳症 | 0 | 0 | 1 (0.2) |
| ラクナ脳卒中 | 1 (0.1) | 0 | 0 |
| 嗜眠 | 1 (0.1) | 1 (0.1) | 0 |
| 記憶障害 | 0 | 2 (0.2) | 0 |
| 片頭痛 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 神経系障害 (Cont.) | | | |
| 神経痛 | 0 | 2 (0.2) | 0 |
| 錯感覚 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 末梢性感覚ニューロパチー | 0 | 2 (0.2) | 0 |
| 睡眠の質低下 | 0 | 0 | 1 (0.2) |
| ヘルペス後神経痛 | 1 (0.1) | 3 (0.4) | 0 |
| 感覚障害 | 0 | 2 (0.2) | 0 |
| 副鼻腔炎に伴う頭痛 | 0 | 0 | 1 (0.2) |
| 傾眠 | 0 | 1 (0.1) | 2 (0.3) |
| 緊張性頭痛 | 1 (0.1) | 0 | 0 |
| 三叉神経障害 | 1 (0.1) | 0 | 0 |
| 三叉神経痛 | 1 (0.1) | 0 | 0 |
| 精神障害 | 6 (0.7) | 7 (0.8) | 6 (1.0) |
| 不安 | 1 (0.1) | 2 (0.2) | 0 |
| 抑うつ気分 | 0 | 0 | 4 (0.6) |
| うつ病 | 1 (0.1) | 2 (0.2) | 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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 精神障害 (Cont.) | | | |
| 不眠症 | 3 (0.4) | 3 (0.4) | 2 (0.3) |
| 睡眠障害 | 1 (0.1) | 0 | 0 |
| 腎および尿路障害 | 8 (1.0) | 14 (1.7) | 11 (1.7) |
| 急性腎障害 | 0 | 1 (0.1) | 0 |
| 尿路結石 | 0 | 1 (0.1) | 0 |
| 慢性腎臓病 | 0 | 1 (0.1) | 0 |
| 腺性膀胱炎 | 1 (0.1) | 0 | 0 |
| 糖尿病性腎症 | 0 | 1 (0.1) | 0 |
| 排尿困難 | 0 | 2 (0.2) | 1 (0.2) |
| 糖尿 | 0 | 0 | 1 (0.2) |
| 血尿 | 2 (0.2) | 4 (0.5) | 3 (0.5) |
| 緊張性膀胱 | 1 (0.1) | 0 | 0 |
| 白血球尿 | 2 (0.2) | 1 (0.1) | 0 |
| 尿意切迫 | 1 (0.1) | 0 | 0 |
| 頻尿 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 腎および尿路障害 (Cont.) | | | |
| 多尿 | 0 | 0 | 1 (0.2) |
| 蛋白尿 | 1 (0.1) | 2 (0.2) | 4 (0.6) |
| 尿路の炎症 | 0 | 0 | 1 (0.2) |
| 生殖系および乳房障害 | 7 (0.8) | 5 (0.6) | 1 (0.2) |
| 無月経 | 1 (0.1) | 1 (0.1) | 1 (0.2) |
| 乳房嚢胞 | 1 (0.1) | 0 | 0 |
| 前立腺結石 | 1 (0.1) | 0 | 0 |
| 勃起不全 | 0 | 1 (0.1) | 0 |
| 線維嚢胞性乳腺疾患 | 0 | 1 (0.1) | 0 |
| 月経過多 | 1 (0.1) | 0 | 0 |
| 不規則月経 | 2 (0.2) | 0 | 0 |
| 不正子宮出血 | 0 | 1 (0.1) | 0 |
| 前立腺炎 | 1 (0.1) | 0 | 0 |
| 陰嚢潰瘍 | 0 | 1 (0.1) | 0 |

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 呼吸器、胸郭および縦隔障害 | 24 (2.9) | 41 (4.9) | 24 (3.8) |
| 喘息 | 0 | 0 | 1 (0.2) |
| カタル | 1 (0.1) | 0 | 0 |
| 咳嗽 | 5 (0.6) | 19 (2.3) | 2 (0.3) |
| 発声障害 | 0 | 1 (0.1) | 0 |
| 呼吸困難 | 2 (0.2) | 1 (0.1) | 1 (0.2) |
| 労作性呼吸困難 | 1 (0.1) | 0 | 0 |
| 鼻出血 | 1 (0.1) | 2 (0.2) | 1 (0.2) |
| 間質性肺疾患 | 0 | 2 (0.2) | 0 |
| 肺浸潤 | 0 | 0 | 1 (0.2) |
| 鼻閉 | 0 | 0 | 2 (0.3) |
| 鼻部不快感 | 1 (0.1) | 0 | 0 |
| 鼻の炎症 | 0 | 1 (0.1) | 0 |
| 鼻潰瘍 | 0 | 1 (0.1) | 0 |
| 口腔咽頭不快感 | 0 | 0 | 1 (0.2) |
| 口腔咽頭痛 | 3 (0.4) | 4 (0.5) | 8 (1.3) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 呼吸器、胸郭および縦隔障害 (Cont.) | | | |
| 咽頭の炎症 | 0 | 1 (0.1) | 1 (0.2) |
| 胸膜炎 | 1 (0.1) | 0 | 0 |
| 肺臓炎 | 0 | 0 | 1 (0.2) |
| 自然気胸 | 0 | 1 (0.1) | 0 |
| 湿性咳嗽 | 0 | 0 | 1 (0.2) |
| 肺塞栓症 | 2 (0.2) | 2 (0.2) | 0 |
| 肺線維症 | 0 | 1 (0.1) | 0 |
| 肺高血圧症 | 1 (0.1) | 0 | 0 |
| 呼吸窮迫 | 1 (0.1) | 0 | 0 |
| アレルギー性鼻炎 | 1 (0.1) | 0 | 0 |
| 鼻漏 | 3 (0.4) | 1 (0.1) | 2 (0.3) |
| 咽喉刺激感 | 0 | 3 (0.4) | 0 |
| 扁桃の炎症 | 0 | 0 | 1 (0.2) |
| 上気道の炎症 | 1 (0.1) | 1 (0.1) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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)

| | UPA | | |
|---|---|---|---|
| System Organ Class<br>MedDRA 22.0 Preferred Term | 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
| 皮膚および皮下組織障害 | 40 (4.8) | 44 (5.2) | 42 (6.7) |
| ざ瘡 | 1 (0.1) | 3 (0.4) | 0 |
| 光線性口唇炎 | 0 | 1 (0.1) | 0 |
| 光線角化症 | 1 (0.1) | 0 | 0 |
| 脱毛症 | 3 (0.4) | 1 (0.1) | 6 (1.0) |
| 水疱 | 1 (0.1) | 4 (0.5) | 0 |
| 肝斑 | 0 | 1 (0.1) | 0 |
| 慢性特発性蕁麻疹 | 1 (0.1) | 0 | 0 |
| 皮膚嚢腫 | 1 (0.1) | 0 | 0 |
| 皮膚炎 | 2 (0.2) | 1 (0.1) | 2 (0.3) |
| ざ瘡様皮膚炎 | 0 | 1 (0.1) | 0 |
| アレルギー性皮膚炎 | 0 | 2 (0.2) | 2 (0.3) |
| アトピー性皮膚炎 | 1 (0.1) | 0 | 0 |
| 皮膚乾燥 | 0 | 1 (0.1) | 0 |
| 異汗性湿疹 | 0 | 1 (0.1) | 0 |
| 湿疹 | 1 (0.1) | 1 (0.1) | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA 15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 皮膚および皮下組織障害 (Cont.) | | | |
| 紅斑 | 0 | 6 (0.7) | 1 (0.2) |
| 環状紅斑 | 0 | 0 | 1 (0.2) |
| 毛髪成長異常 | 1 (0.1) | 0 | 0 |
| 多汗症 | 2 (0.2) | 0 | 0 |
| 嵌入爪 | 0 | 0 | 2 (0.3) |
| 間擦疹 | 2 (0.2) | 0 | 0 |
| 爪郭の炎症 | 0 | 1 (0.1) | 0 |
| 爪成長異常 | 1 (0.1) | 0 | 0 |
| 爪破損 | 1 (0.1) | 0 | 0 |
| 爪甲剥離症 | 0 | 1 (0.1) | 0 |
| 丘疹 | 0 | 1 (0.1) | 1 (0.2) |
| 光線過敏性反応 | 0 | 0 | 1 (0.2) |
| そう痒症 | 0 | 1 (0.1) | 6 (1.0) |
| 全身性そう痒症 | 1 (0.1) | 0 | 1 (0.2) |
| 乾癬 | 6 (0.7) | 6 (0.7) | 7 (1.1) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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)

| | UPA | | |
|---|---|---|---|
| | 15 mg QD (N = 617) (PYs = 839.1) | 30 mg QD (N = 613) (PYs = 842.8) | ADA 40 mg EOW (N = 429) (PYs = 631.4) |
| System Organ Class<br>MedDRA 22.0 Preferred Term | Events (E/100 PYs) | Events (E/100 PYs) | Events (E/100 PYs) |
| 皮膚および皮下組織障害 (Cont.) | | | |
| 膿疱性乾癬 | 0 | 1 (0.1) | 0 |
| 発疹 | 2 (0.2) | 7 (0.8) | 3 (0.5) |
| 紅斑性皮疹 | 0 | 0 | 1 (0.2) |
| 毛孔性皮疹 | 1 (0.1) | 0 | 1 (0.2) |
| 全身性皮疹 | 1 (0.1) | 0 | 2 (0.3) |
| 斑状皮疹 | 2 (0.2) | 1 (0.1) | 0 |
| 斑状丘疹状皮疹 | 1 (0.1) | 0 | 1 (0.2) |
| 酒さ | 2 (0.2) | 0 | 0 |
| 皮膚剥脱 | 0 | 1 (0.1) | 0 |
| 皮膚刺激 | 1 (0.1) | 1 (0.1) | 0 |
| 皮膚病変 | 3 (0.4) | 0 | 0 |
| 顔面腫脹 | 1 (0.1) | 0 | 0 |
| 蕁麻疹 | 0 | 0 | 3 (0.5) |
| 社会環境 | 0 | 0 | 1 (0.2) |
| 中年の転換期 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
E/100 PYs = Events per 100 patient-years.

Program Source Code: [redacted]

TABLE 14.3__1.3

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<br>MedDRA 22.0 Preferred Term | UPA<br>15 mg QD<br>(N = 617)<br>(PYs = 839.1)<br>Events<br>(E/100 PYs) | UPA<br>30 mg QD<br>(N = 613)<br>(PYs = 842.8)<br>Events<br>(E/100 PYs) | ADA 40 mg EOW<br>(N = 429)<br>(PYs = 631.4)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 血管障害 | 15 (1.8) | 9 (1.1) | 9 (1.4) |
| 深部静脈血栓症 | 2 (0.2) | 0 | 0 |
| 血腫 | 0 | 0 | 1 (0.2) |
| ほてり | 3 (0.4) | 0 | 0 |
| 高血圧 | 8 (1.0) | 8 (0.9) | 3 (0.5) |
| 高血圧クリーゼ | 1 (0.1) | 0 | 0 |
| リンパ浮腫 | 0 | 0 | 1 (0.2) |
| レイノー現象 | 0 | 0 | 1 (0.2) |
| 血栓性静脈炎 | 1 (0.1) | 0 | 1 (0.2) |
| 表在性血栓性静脈炎 | 0 | 1 (0.1) | 1 (0.2) |
| 血管炎 | 0 | 0 | 1 (0.2) |

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 and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg 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 |
|---|---|---|---|---|
| 変形性関節症 | X | | | |
| 肺塞栓症 | X | X | | X |

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

| Medical History | Onset Year |
|---|---|
| OTHER: PLAQUE PSORIASIS | 19[redacted] |
| OTHER: APPENDECTOMY | 19[redacted] |
| OTHER: HEADACHES | 19[redacted] |
| CANCER: BASAL CELL CARCINOMA | 20[redacted] |
| OTHER: OBESITY | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| SLEEP APNEA | 20[redacted] |
| OTHER: HYPERLIPIDEMIA | 20[redacted] |
| OTHER: INSOMNIA | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: MULTIPLE LEFT ARM FRACTURES | 20[redacted] |
| DRUG ALLERGIES/REACTIONS: METHOTREXATE ALLERGY | 20[redacted] |
| OTHER: BLADDER INFECTIONS | 20[redacted] |
| OTHER: BENIGN THYROID NODULE | 20[redacted] |
| DEGENERATIVE DISC DISEASE: CERVICAL, THORACIC, AND LUMBAR | 20[redacted] |
| OSTEOARTHRITIS | 20[redacted] |
| OTHER: BILATERAL HEEL SPURS | 20[redacted] |
| OTHER: SHORTNESS OF BREATH | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: CHOLECYSTECTOMY | 19[redacted] |
| SURGERY: HYSTERECTOMY | 19[redacted] |
| SURGERY: GASTRIC BANDING | 20[redacted] |
| SURGERY: REMOVAL OF GASTRIC BAND | 20[redacted] |
| SURGERY: REMOVAL OF LEFT THYROID NODULE | 20[redacted] |

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

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted] / 1 | [redacted] / 164 | 164 |
| ABT-494 | 30 MG | ORAL | QD | [redacted] / 165 | [redacted] / 394 | 230 |
| ABT-494 | 30 MG | ORAL | QD | [redacted] / 395 | [redacted] / 712 | 318 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| IBUPROFEN | 200 mg | BID | Y-M: 20[redacted] |
| AMLODIPINE | 5 mg | QD | Y-M: 20[redacted] |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] |
| DYAZIDE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] |
| HYDROXYZINE | 25 mg | QD | Y-M: 20[redacted] |
| LISINOPRIL | 20 mg | QD | Y-M: 20[redacted] |
| METHOTREXATE | 10 mg | EVERY WEEK | Y-M: 20[redacted] |
| CENTRUM | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -87 |

**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 | 200 mg | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 505 |
| AMLODIPINE | 5 mg | QD | Y-M: 20[redacted] | ONGOING |
| DYAZIDE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] | ONGOING |
| LISINOPRIL | 20 mg | QD | Y-M: 20[redacted] | ONGOING |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 493 |
| HYDROXYZINE | 25 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 497 |
| CENTRUM | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -87 | ONGOING |
| MUPIROCIN | 2 % | BID | Y-M: 20[redacted] / 217 | Y-M: 20[redacted] / 228 |
| VALACICLOVIR | 1000 mg | TID | Y-M: 20[redacted] / 224 | Y-M: 20[redacted] / 232 |
| LIDOCAINE | 2 mL | OTHER: SINGLE DOSE | Y-M: 20[redacted] / 352 | Y-M: 20[redacted] / 352 |
| ROPIVACAINE | 2 mL | OTHER: SINGLE DOSE | Y-M: 20[redacted] / 352 | Y-M: 20[redacted] / 352 |
| TRIAMCINOLONE | 80 mg | OTHER: SINGLE DOSE | Y-M: 20[redacted] / 352 | Y-M: 20[redacted] / 352 |
| ISOSORBIDE MONONITRATE | 10 mg | BID | Y-M: 20[redacted] / 377 | Y-M: 20[redacted] / 493 |

| | | | | |
|---|---|---|---|---|
| VALACICLOVIR | 1000 g | TID | Y-M: 20[redacted] / 384 | Y-M: 20[redacted] / 390 |
| VALACICLOVIR | 1000 g | QD | Y-M: 20[redacted] / 391 | Y-M: 20[redacted] / 687 |
| ANESTHETICS, GENERAL | UNKNOWN OTHER: UNKNOWN | OTHER: SINGLE DOSE | Y-M: 20[redacted] / 457 | Y-M: 20[redacted] / 457 |
| CEFAZOLIN | UNKNOWN OTHER: UNKNOWN | OTHER: SINGLE DOSE | Y-M: 20[redacted] / 457 | Y-M: 20[redacted] / 457 |
| MACROGOL 3350 | 1 OTHER: TABLET | PRN | Y-M: 20[redacted] / 458 | Y-M: 20[redacted] / 465 |
| VICODIN | 7.5/325 mg | PRN | Y-M: 20[redacted] / 458 | Y-M: 20[redacted] / 485 |
| ACETYLSALICYLIC ACID | 81 mg | BID | Y-M: 20[redacted] / 458 | Y-M: 20[redacted] / 486 |
| DOCUSATE | 1 OTHER: TABLET | PRN | Y-M: 20[redacted] / 466 | NOT REPORTED |
| NAPROXEN | 500 mg | QD | Y-M: 20[redacted] / 569 | NOT REPORTED |
| ACICLOVIR | 800 mg | QD | Y-M: 20[redacted] / 687 | ONGOING |
| FUROSEMIDE | 40 mg | QD | Y-M: 20[redacted] / 687 | ONGOING |
| LEVOTHYROXINE | 0.05 mg | QD | Y-M: 20[redacted] / 687 | ONGOING |
| HEPARIN | 8300 IU | OTHER: ONCE | Y-M: 20[redacted] / 713 | Y-M: 20[redacted] / 713 |
| IOPAMIDOL | 79 OTHER: CC | OTHER: SINGLE DOSE | Y-M: 20[redacted] / 713 | Y-M: 20[redacted] / 713 |
| HEPARIN | 3800 IU | OTHER: ONCE | Y-M: 20[redacted] / 714 | Y-M: 20[redacted] / 714 |
| APIXABAN | 5 mg | BID | Y-M: 20[redacted] / 715 | ONGOING |
| APIXABAN | 10 mg | BID | Y-M: 20[redacted] / 715 | Y-M: 20[redacted] / 721 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING OF OSTEOARTHRITIS RIGHT HIP |
| **Preferred term** | 変形性関節症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 157 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 457): REBOTICALLY ASSISTED AND CT-GUIDED PATIENT SPECIFIC CEMENTLESS RIGHT TOTAL HIP ARTHROPLASTY.: PATIENT AT HOME AND CURRENTLY RECEIVING PHYSICAL THERAPY AT HER HOME.

| | |
|---|---|
| **AE Stopped Rx Day** | 458 |
| **Duration of AE** | 302 DAYS |

| | |
|---|---|
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | SEVERE OSTEOARTHRITIS AND SHE HAS FAILED SEVERAL ATTEMPTS AT CONSERVATIVE TREATMENT. |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

**Event #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Cardiovascular Events**

| | |
|---|---|
| **Event Description** | PULMONARY EMBOLISM BILATERAL |
| **Preferred term** | 肺塞栓症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 713 (1 DAY AFTER LAST TREATMENT) |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 713): Chloride: 108 [98 - 107] MMOL/L; Erythrocytes: 3.5 [3.8 - 5.8] 10^12/L; Hematocrit: 0.34 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 116 [117 - 161] G/L; NPTST224-D-DIMER: 748 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST480-NTPROBNP: 59 [NOT REPORTED - NOT REPORTED] PG/ML; NPTST651-TROPONIN-I: .012 [NOT REPORTED - 0.034] ng/mL; Prothrombin Intl. Normalized Ratio: 1 [0.9 - 1.2] RATIO; [redacted]20[redacted] (RX DAY 714): Erythrocytes: 3.4 [3.8 - 5.8] 10^12/L; Hematocrit: 0.33 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 111 [117 - 161] G/L; NPTST091-BASELINE LA PTT: 157.8 [33.2 - 40.6] SEC; NPTST257-FACTOR 8: 216 [50 - 150] %; NPTST530-PROTEIN C FUNC: 145 [70 - 130] %; NPTST625-THROMBIN TIME MHC: 120 [14.1 - 17] SEC; [redacted]20[redacted] (RX DAY 715): Erythrocytes: 3.7 [3.8 - 5.8] 10^12/L

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 713): CTA CHEST WITH AND WITHOUT CONTRAST: MULTIPLE BILATERAL PULMONARY EMBOLI, MORE PROMINENT IN THE RIGHT LUNG. 6MM RIGHT UPPER LOBE PULMONARY NODULE.; ECG: NORMAL SINUS RHYTHM, NONSPECIFIC ST ABNORMALITY, ABNORMAL ECG; [redacted]20[redacted] (RX DAY 714): CT ABDOMEN AND PELVIS WITHOUT INFUSION: NO ACUTE ABNORMALITIES, SMALL HIATAL HERNIA, VENOUS COMPRESSION DEFORMITY, SCATTERED DIVERTICULA IN THE LEFT COLON; ECHOCARDIOGRAM: LEFT VENTRICULAR HYPERTROPHY, MITRAL VALVE MILD REGURGITATION.; LOWER EXTREMITY VENOUS DOPPLER: NO EVIDENCE OF OBSTRUCTIVE THROMBUS IN THE VISUALIZED LOWER EXTREMITY DEEP VEINS RIGHT OR LEFT.

| | |
|---|---|
| **AE Stopped Rx Day** | 715 (3 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 3 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，右股関節の変形性関節症の悪化の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，局面型乾癬，睡眠時無呼吸，乾癬性関節炎，多発性左腕骨折，両側性踵骨棘，頚椎，胸椎及び腰椎の椎間板変性疾患，変形性関節症，息切れ及び非喫煙者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤が投与されたのは 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月，被験者は右股関節の変形性関節症の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右股関節の変形性関節症の悪化は消失した。

右股関節痛の悪化が数ヵ月続いていた。これは急速に悪化し，持続していた。右股関節痛は，両側臀部に及ぶ中等度から重度の刺すような鋭い疼痛であった。被験者は保存的治療を数回試したが，改善には至らなかった。被験者は人工股関節全置換術を受けることにした。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は，引っかかり感，可動域減少，椅子からの立ち上がりが困難，靴下や靴を履くのが困難，摩擦感，ひきずり足歩行，関節の固まり，こわばり感及び脱力といった随伴症状を訴えた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はロボット支援 CT ガイド下セメントレス右人工股関節置換術を受けた。手術所見は，重度の右大腿骨頭及び右寛骨臼表面の変形であった。被験者は手術に十分耐えた。被験者は，術後とその後 24 時間，アスピリンと抗生物質を予防的に投与された。間欠的空気圧迫装置の使用，大腿部までの長さの TED ソックスの使用，静脈血栓塞栓症予防のための早期モビライゼーション及び許容範囲内のウェイトベアリングが開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，理学療法を継続することとなった。

投与された薬剤は，ロピバカイン，ancef，norco，リドカイン，kenalog 及び naprosyn であった。

**The patient's past medications include:**

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

Causality for UPADACITINIB (Blinded)

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1) Osteoarthritis aggravated (10031162) (Osteoarthritis (10031161) ) [v.22.1] [10031162]

**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)

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Event of WORSENING OF OSTEOARTHRITIS RIGHT HIP

**- Investigator:** SEVERE OSTEOARTHRITIS AND SHE HAS FAILED SEVERAL ATTEMPTS AT CONSERVATIVE TREATMENT

**- AbbVie:** risk factors include pre-existing osteoarthritis and advanced age.

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，両側肺塞栓症の事象を発現した。

**Event 3 の臨床経過：**

関連する病歴は，局面型乾癬，肥満，高血圧，睡眠時無呼吸，高脂血症，乾癬性関節炎，変形性関節症，息切れ，非喫煙者及び飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 9 日，被験者は両側肺塞栓症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，両側肺塞栓症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，特に 3 週間に及ぶ歩行時の息切れ（SOB）／呼吸困難（非重篤）の増加により，外来を受診した。これらの症状は徐々に悪化した。時折，胸部不快感があった。被験者によれば，下肢の痛みや腫れ，咳はないとのことであった。D ダイマー増加が認められ，被験者は救急治療室（ER）を受診するよう指示された。被験者は ER を受診した。CT 血管造影で両側肺塞栓症（PE）が明らかとなり，そのまま入院した。PE は右肺上葉でより顕著であり，右肺上葉小結節（非重篤）も認められた。被験者によれば，ここ最近の手術歴及び旅行歴はなく，運動不能な状態でもなかった。また被験者によれば，PE 及び深部静脈血栓症（DVT）の病歴はなく，血液凝固障害の家族歴もなかった。ヘパリンのボーラス投与及び点滴が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，肺診察時に被験者の睡眠時無呼吸と CPAP 開始の必要性について説明が行われた。診察時において，被験者には，デスクワークをはじめ，比較的体を動かすことの少ない生活であること以外には，明確な増悪因子が存在しないことがわかった。そのため，抗凝固療法期間を少なくとも最長で 3 年に延長することを検討する必要があった。腹腔内に大きな疾患が存在する可能性を排除するため，両側静脈ドップラー超音波検査および腹部 CT スキャンが行われた。入院中，ヘパリン点滴は経口抗凝固薬エリキュース 10 mg 1 日 2 回に切り替えられた。被験者は室内気下で問題なく歩き回っており，酸素飽和度は 90%超で維持されていた。被験者によれば，さらなる SOB／呼吸困難はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，医師による経過観察を受けることとなった。

本事象により治験薬の投与が完全に中止された。

投与された薬剤は，エリキュース及びヘパリンであった。

**The patient's past medications include:**

MOTRIN foPSORIATIC ARTHRITIS (20[redacted] - [redacted] [redacted] 20[redacted])

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

Causality for UPADACITINIB (Blinded)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377) ) [v.22.1] [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

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of PULMONARY EMBOLISM BILATERAL

**- Investigator:** Not applicable

**- AbbVie:** Risk factors include pre-existing psoriasis, obesity and advanced age.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BASELINE LA PTT:** 157.8 SEC (normal 33.2 to 40.6)

[redacted] **20[redacted] BMI:** 41.8 kg/m2

[redacted] **20[redacted] CHEST X-RAY:** screening: normal

[redacted] **20[redacted] CHLORIDE:** 108 MEQ/L (normal 98 to 107)

[redacted] **20[redacted] CT ABDOMEN:** No acute abnormalities, Small hiatal hernia, venous compression deformity, scattered diverticula in the left colon (non-serious)

[redacted] **20[redacted] CT ANGIOGRAM CHEST:** Multiple bilateral pulmonary emboli, more prominent in the right lung. 6mm right upper lobe pulmonary nodule (non-serious)

[redacted] **20[redacted] D-DIMER:** 748 no unit

[redacted] **20[redacted] ECG:** Normal sinus rhythm, nonspecific ST abnormality, abnormal ECG

[redacted] **20[redacted] ECHOCARDIOGRAM:** Left ventricular hypertrophy, Mitral valve mild regurgitation

[redacted] **20[redacted] FACTOR 8 TEST:** 216 % (normal 50 to 150)

[redacted] **20[redacted] HEMATOCRIT:** 33.8 % (normal 35.0 to 47.0)

[redacted] **20[redacted] HEMATOCRIT:** 32.7 % (normal 35.0 to 47.0)

[redacted] **20[redacted] HEMOGLOBIN:** 11.6 G/DL (normal 11.7 to 16.1)

[redacted] **20[redacted] INTERNATIONAL NORMALIZED RATIO:** 1.0 ratio (normal 0.9 to 1.2)

[redacted] **20[redacted] LOWER EXTREMITY VENOUS DOPPLER:** No evidence of obstructive thrombus in the visualized lower extremity deep veins right or left

[redacted] **20[redacted] NTPRO BNP:** 59 PG/ML

[redacted] **20[redacted] OXYGEN SATURATION:** >90%

[redacted] **20[redacted] PROTEIN C FUNCTION:** 145 % (normal 70 to 130)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.54 M/mcl (normal 3.80 to 5.80)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.44 M/mcl (normal 3.80 to 5.80)

[redacted] **20[redacted] THROMBIN TIME MHC:** > 120.0 seconds

[redacted] **20[redacted] TROPONIN I:** .012 NG/ML (normal 0.000 to 0.034)

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 |
|---|---|---|---|---|
| 脱髄 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 30 mg QD | 3[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| CHOLECYSTITIS | 20[redacted] |
| OTHER: HEADACHES | 20 |
| OBESITY | 20 |
| OTHER: PLAQUE PSORIASIS | 20 |
| PSORIATIC ARTHRITIS | 20 |
| OTHER: DEMYELINATING DISEASE | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| Not reported. | |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 36 | 36 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| METHOTREXATE | 15 mg | QD | Y-M: 20[redacted] |
| CYANOCOBALAMIN | 1 OTHER: TAB | QD | Y-M: 20[redacted] |
| IBUPROFEN | 800 mg | QD | Y-M: 20[redacted] |
| PYRIDOXINE | 1 OTHER: TAB | QD | Y-M: 20[redacted] |
| TRAMADOL | 50 mg | QD | Y-M: 20[redacted] |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted] / -46 |

**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 |
|---|---|---|---|---|
| CYANOCOBALAMIN | 1 OTHER: TAB | QD | Y-M: 20[redacted] | ONGOING |
| IBUPROFEN | 800 mg | QD | Y-M: 20[redacted] | ONGOING |
| PYRIDOXINE | 1 OTHER: TAB | QD | Y-M: 20[redacted] | ONGOING |
| TRAMADOL | 50 mg | QD | Y-M: 20[redacted] | ONGOING |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted] / -46 | ONGOING |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 16 | ONGOING |
| DIPHENHYDRAMINE | 25 mg | OTHER: ONCE | Y-M: 20[redacted] / 16 | Y-M: 20[redacted] / 16 |
| HYDROMORPHONE | 0.5 mg | TID | Y-M: 20[redacted] / 16 | Y-M: 20[redacted] / 16 |
| METHYLPREDNISOLONE | 250 mg | TID | Y-M: 20[redacted] / 16 | Y-M: 20[redacted] / 16 |
| METOCLOPRAMIDE | 10 mg | OTHER: ONCE | Y-M: 20[redacted] / 16 | Y-M: 20[redacted] / 16 |
| PREDNISONE | 50 mg | QD | Y-M: 20[redacted] / 16 | Y-M: 20[redacted] / 27 |

**Event #1: Serious Adverse Event**

**Event Description** DEMYELINATING DISEASE FLARE

**Preferred term** 脱髄

**AE Onset Date / Rx Day** [redacted]20[redacted] / 16

**Age at AE Onset** 3[redacted]

**Laboratory Testing**

NOT REPORTED

**Microbiology**

[redacted]20[redacted] (RX DAY 17): CEREBROSPINAL FLUID NPTST416-LUMBAR PUNCTURE: Negative

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 16): MRI BRAIN W/ +W/O CONTRAST: 1. REDEMONSTRATED NUMEROUS SUPRATENTORIAL WHITE MATTER LESIONS, NONSPECIFIC BUT SIGNIFICANTLY GREATER THAN EXPECTED FOR AGE. THE MAJORITY OF LESIONS APPEAR SIMILAR TO THE PRIOR STUDY, ALTHOUGH A FEW LESIONS APPEAR SLIGHTLY INCREASED IN CONSPICUITY AND A FEW LESIONS APPEAR SLIGHTLY DECREASED IN CONSPICUITY. FINDINGS PRESUMABLY RELATE TO THE PATIENT'S HISTORY OF DEMYELINATING DISEASE. NO ENHANICINGLESION IS IDENTIFIED TO SUGGEST ACTIVE DEMYELINATION 2 NO ACUTE INFARCTION OR HEMORRAGE; [redacted]20[redacted] (RX DAY 17): FL LUMBAR PUNCTURE: RESULTS NO OLIGOCLONAL BANDS CSF PROTEIN LEVEL WAS NORMAL; MRI SPINE CERVICAL W/ + W/O CONTRAST: NO MRI FEATURES OF DEMYELINATING DISEASE EARLY DEGENERATIVE SPONDYLOSIS. NO SIGNIFICANT CANAL STENOSIS NO FORAMINAL NARROWING

**AE Stopped Rx Day** 20

**Duration of AE** 5 DAYS

**Severity** Moderate

**Relation to Study Drug by Investigator** No Reasonable Possibility

| | |
|---|---|
| **Investigator Alternative Etiology** | [redacted] 20[redacted] SHE HAD WORKUP FOR WEAKNESS |
| **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:** M15-572

治験責任医師からの報告。本被験者は米国の 3[redacted] 歳女性であり，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，脱髄性疾患の再燃の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，肥満，局面型乾癬，乾癬性関節炎，脱髄性疾患，非喫煙者，禁酒及び多発性硬化症疑いの病歴であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は脱髄性疾患の再燃を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，脱髄性疾患の再燃は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は救急科を受診し，「あちこちの」痛み，頭痛，脱力，歩行困難，発話困難，手指関節痛（大抵は午前中に出現し，1 日中持続）などを訴えた。被験者は，過去数ヵ月間にわたって進行性の脱力及び歩行困難があったと述べた。また被験者は，物を落としたり，日常生活動作を行うことができずに欠勤したりしたことを報告した。身体的診察で MCP 関節腫脹及び両膝・両肘・腹部の多発性局面型乾癬が認められた。その後，被験者は精査及び管理のため入院した。神経学的診察が完了した。20[redacted] 年 [redacted] 月 [redacted] 日，神経学医は脱髄性症候群と多発性硬化症（MS）の鑑別が必要であると暫定的に判断した。脊椎穿刺，転倒の評価及び頚椎 MRI の実施が推奨されるとともに，ソルメドロール（メチルプレドニゾロン）250 mg TID 2 日間の投与が開始された。腰椎穿刺でオリゴクローナルバンドは存在しないことが確認された。理学療法が追加で指示された。20[redacted] 年 [redacted] 月 [redacted] 日，神経学医の印象では，結合組織障害で見られることがある脱髄性症候群の可能性が高く，MS に典型的な所見ではなかった（CSF 検査も陰性）。入院中，被験者の症状は改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，神経学医による経過観

察を受けることとなった。

被験者は本治験を中止した。

投与された薬剤は，dilaudid，オンダンセトロン及びソル・メドロールであった。

Causality for UPADACITINIB (Blinded)

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1) Demyelination (10012305) (Demyelination (10012305) ) [v.22.1] [10012305]

**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 DEMYELINATING DISEASE FLARE

**- Investigator:** [redacted] 20[redacted]: The patient had a work-up for weakness.

**- AbbVie:** Reported event is more likely related to pre-existing Demyelinating disease associated with abnormal MRI finding ([redacted] 20[redacted])

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BLOOD PRESSURE:** 142/80mmHg

[redacted] **20[redacted] CREATININE:** 0.5 no unit

[redacted] **20[redacted] EKG:** Normal sinus rhythm. 74bpm. Nonspecific T waves. No ST elevation or depression. QTc 435ms.

[redacted] **20[redacted] FL LUMBAR PUNCTURE:** Results no oligoclonal bands CSF protein level was normal.

[redacted] **20[redacted] GLUCOSE:** 126 no unit

[redacted] **20[redacted] HGB:** 12.4 no unit

**20[redacted] LUMBAR PUNCTURE:** Positive for oligoclonal bands.

[redacted] **20[redacted] MRI BRAIN:** Numerous supratentorial white matter hyperintensities which was presumed to be related to demyelinating disease. No acute infarction or hemorrhage.

[redacted] **20[redacted] MRI BRAIN W/ +W/O CONTRAST:** 1. Redemonstrated numerous supratentorial white matter lesions, nonspecific but significantly greater than expected for age. The majority of lesions appear similar to the prior study, although a few lesions appear slightly increased in conspicuity and a few lesions appear slightly decreased in conspicuity. Findings presumably relate to the patient's history of demyelinating disease. No enhancing lesion is identified to suggest active demyelination. 2. No acute infarction or hemorrhage.

[redacted] **20[redacted] MRI LUMBAR SPINE:** Degenerative joint disease and moderate bulging disk.

[redacted] **20[redacted] MRI SPINE CERVICAL W/ + W/O CONTRAST:** No MRI features of demyelinating disease; early degenerative spondylosis. No significant canal stenosis no foraminal narrowing.

[redacted] **20[redacted] PLT:** 277 no unit

[redacted] **20[redacted] POTASSIUM:** 3.5 no unit

[redacted] **20[redacted] SODIUM:** 138 no unit

[redacted] **20[redacted] SPO2:** 99 %

[redacted] **20[redacted] TSH:** 2.38 no unit

[redacted] **20[redacted] WBC:** 9.2 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 |
|---|---|---|---|---|
| 憩室炎 | X | | | X |
| 上部消化管出血 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 15 mg QD | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: CYST ON VOCAL CORDS | 19[redacted] |
| HYPERTENSION | 19[redacted] |
| OTHER: POST MENOPAUSAL | 19[redacted] |
| GOUT: HISTORY OF GOUT-INACTIVE | 20[redacted] |
| COGNITIVE OR PSYCHIATRIC DISORDER: INSOMNIA | 20[redacted] |
| DIABETES MELLITUS: TYPE II | 20[redacted] |
| OTHER: DIABETIC NEUROPATHY | 20[redacted] |
| ANEMIA: LACK OF HEALTHY RED BLOOD CELLS | 20[redacted] |
| GASTROINTESTINAL BLEED: BLEEDING IN THE INTESTINE | 20[redacted] |
| MYOCARDIAL INFARCTION | 20[redacted] |
| OTHER: HERNIATED DISKS LOWER BACK | 20[redacted] |
| CONGESTIVE HEART FAILURE | 20[redacted] |
| MYOCARDIAL INFARCTION | 20[redacted] |
| COGNITIVE OR PSYCHIATRIC DISORDER: ANXIETY | 20[redacted] |
| HYPOTHYROIDISM | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: CKE-STAGE 3 | 20[redacted] |
| OTHER: HYPERCHOLESTEROLEMIA | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: TRACHEOTOMY | 19[redacted] |
| SURGERY: C-SECTION | 19[redacted] |
| SURGERY: TUBAL LIGATION | 19[redacted] |
| SURGERY: LEFT HIP REPLACED | 20[redacted] |
| SURGERY: RT HIP REPLACED | 20[redacted] |
| SURGERY: LFT KNEE REPLACED | 20[redacted] |

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

| | |
|---|---|
| E-CIGARETTES | NEVER |
| PIPES | NEVER |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 1 | [redacted] / 171 | 171 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 172 | [redacted] / 221 | 50 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| GABAPENTIN | 600 mg | TID | Y-M: 20[redacted] |
| ALLOPURINOL | 100 mg | QD | Y-M: 20[redacted] |
| HEPATITIS B IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| TRAZODONE | 150 mg | QD | Y-M: 20[redacted] |
| FUROSEMIDE | 40 mg | QD | Y-M: 20[redacted] |
| INSULIN ASPART | 40 OTHER: UNITS | BID | Y-M: 20[redacted] |
| RISTFOR | 50/1000 mg | BID | Y-M: 20[redacted] |
| ATORVASTATIN | 10 mg | QD | Y-M: 20[redacted] |
| IBUPROFEN | 600 mg | TID | Y-M: 20[redacted] / -352 |
| LEVOTHYROXINE | .025 mg | QD | Y-M: 20[redacted] / -352 |
| NAPROXEN | 500 mg | BID | Y-M: 20[redacted] / -352 |
| CITALOPRAM | 20 mg | QD | Y-M: 20[redacted] / -168 |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -168 |
| METHOTREXATE | 7.5 mg | EVERY WEEK | 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 |
|---|---|---|---|---|
| GABAPENTIN | 600 mg | TID | Y-M: 20[redacted] | ONGOING |
| TRAZODONE | 150 mg | QD | Y-M: 20[redacted] | ONGOING |
| FUROSEMIDE | 40 mg | QD | Y-M: 20[redacted] | ONGOING |
| INSULIN ASPART | 40 OTHER: UNITS | BID | Y-M: 20[redacted] | ONGOING |
| RISTFOR | 50/1000 mg | BID | Y-M: 20[redacted] | ONGOING |
| ATORVASTATIN | 10 mg | QD | Y-M: 20[redacted] | ONGOING |
| LEVOTHYROXINE | .025 mg | QD | Y-M: 20[redacted] / -352 | ONGOING |
| IBUPROFEN | 600 mg | TID | Y-M: 20[redacted] / -352 | Y-M: 20[redacted] / 181 |
| NAPROXEN | 500 mg | BID | Y-M: 20[redacted] / -352 | Y-M: 20[redacted] / 181 |
| CITALOPRAM | 20 mg | QD | Y-M: 20[redacted] / -168 | ONGOING |

| | | | | |
|---|---|---|---|---|
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / - 168 | ONGOING |
| METHOTREXATE | 7.5 mg | EVERY WEEK | Y-M: 20[redacted] / - 168 | ONGOING |
| NITROFURANTOIN | 100 mg | BID | Y-M: 20[redacted] / 144 | Y-M: 20[redacted] / 171 |
| BISMUTH | 17.6 mg | PRN | Y-M: 20[redacted] / 168 | ONGOING |
| LOPERAMIDE | 2 mg | PRN | Y-M: 20[redacted] / 168 | ONGOING |
| BLOOD AND RELATED PRODUCTS | 2 OTHER: UNITS | OTHER: ONCE | Y-M: 20[redacted] / 177 | Y-M: 20[redacted] / 177 |
| ONDANSETRON | 4 mg | OTHER: ONCE | Y-M: 20[redacted] / 177 | Y-M: 20[redacted] / 177 |
| PANTOPRAZOLE | 80 mg | OTHER: ONCE | Y-M: 20[redacted] / 177 | Y-M: 20[redacted] / 177 |
| PIPERACILLIN W/TAZOBACTAM | 100 mL | OTHER: ONCE | Y-M: 20[redacted] / 177 | Y-M: 20[redacted] / 177 |
| SODIUM CHLORIDE | 500 mL | OTHER: ONCE | Y-M: 20[redacted] / 177 | Y-M: 20[redacted] / 177 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 179 | ONGOING |
| SUCRALFATE | 1 g | QID | Y-M: 20[redacted] / 179 | ONGOING |
| TRAMADOL | 50 mg | QID | Y-M: 20[redacted] / 181 | ONGOING |
| CIPROFLOXACIN | 400 mg | OTHER: ONCE | Y-M: 20[redacted] / 238 | Y-M: 20[redacted] / 238 |
| METRONIDAZOLE | 500 mg | OTHER: ONCE | Y-M: 20[redacted] / 238 | Y-M: 20[redacted] / 238 |
| ONDANSETRON | UNKNOWN OTHER: UNKNOWN | OTHER: UNKNOWN | Y-M: 20[redacted] / 238 | Y-M: 20[redacted] / 238 |
| PANADEINE CO | 30/300 mg | PRN | Y-M: 20[redacted] / 238 | Y-M: 20[redacted] / 238 |
| RED BLOOD CELLS | 1 OTHER: UNIT | OTHER: ONCE | Y-M: 20[redacted] / 238 | Y-M: 20[redacted] / 238 |
| SODIUM CHLORIDE | UNKNOWN OTHER: UNKNOWN | OTHER: UKNOWN | Y-M: 20[redacted] / 238 | Y-M: 20[redacted] / 238 |
| LABETALOL | UNKNOWN OTHER: UNKNOWN | PRN | Y-M: 20[redacted] / 238 | Y-M: 20[redacted] / 253 |
| PLATELETS | 1 OTHER: UNIT | OTHER: ONCE | Y-M: 20[redacted] / 244 | Y-M: 20[redacted] / 244 |
| RED BLOOD CELLS | 2 OTHER: UNITS | OTHER: ONCE | Y-M: 20[redacted] / 244 | Y-M: 20[redacted] / 244 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | UPPER GI BLEED |
| **Preferred term** | 上部消化管出血 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 177 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |

[redacted]20[redacted] (RX DAY 177): Albumin: 31 [36 - 51] G/L; Blood Urea Nitrogen: 16.8 [2.1 - 8.6] MMOL/L; Creatinine: 133 [44 - 88] UMOL/L; Erythrocytes: 2.4 [3.9 - 5] 10^12/L; Hematocrit: 0.24 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 77 [120 - 155] G/L; Leukocytes: 13.4 [4.8 - 10.8] 10^9/L; NPTST010-A/G RATIO: 1 [1.5 - 2.5] RATIO; NPTST116-BNP: 155 [0 - 100] PG/ML; NPTST263-FECAL OCCULT BLOOD: POSITIVE [0 - 0] POSITIVE OR NEGATIVE, NO UNITS; NPTST402-LACTIC ACID: 3.1 [0 - 2] MMOL/L; NPTST428-MCHC: 32.4 [33.4 - 35.5] G/DL; NPTST429-MCV: 100.4 [82.5 - 98] FL; NPTST538-PROTIME: 12.7 [9.5 - 12.5] SEC; NPTST562-RDW: 16.7 [11.8 - 15.6] %; NPTST646-TROPONIN I: 0.05 [0 - 0.04] NG/ML; Neutrophils: 10.3 [1.7 - 7] 10^9/L; Protein: 62 [64 - 84] G/L; [redacted]20[redacted] (RX DAY 178): Blood Urea Nitrogen: 14.3 [2.1 - 8.6] MMOL/L; Calcium: 2.05 [2.15 - 2.59] MMOL/L; Chloride: 112 [98 - 110] MMOL/L; Creatinine: 141 [44 - 88] UMOL/L; Hematocrit: 0.26 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 83 [120 - 155] G/L; [redacted]20[redacted] (RX DAY 179): Blood Urea Nitrogen: 13.2 [2.1 - 8.6] MMOL/L; Calcium: 1.95 [2.15 - 2.59] MMOL/L; Creatinine: 150 [44 - 88] UMOL/L; Erythrocytes: 2.5 [3.9 - 5] 10^12/L; Hematocrit: 0.25 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 83 [120 - 155] G/L; Leukocytes: 10.9 [4.8 - 10.8] 10^9/L; NPTST562-RDW: 17.6 [11.8 - 15.6] %; [redacted]20[redacted] (RX DAY 180): Erythrocytes: 2.5 [3.9 - 5] 10^12/L; Hematocrit: 0.24 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 79 [120 - 155] G/L; NPTST428-MCHC: 32.8 [33.4 - 35.5] G/DL; NPTST562-RDW: 17.3 [11.8 - 15.6] %

**Microbiology**

[redacted]20[redacted] (RX DAY 179): OTHER STOMACH BX NPTST499-PATHOLOGY EXAM: Not applicable-ACTIVE EROSIVE GASTRITIS; NO HELICOBACTERPYLORI ORGANISMS IDENTIFIED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 177): CT ABDOMEN PELVIS WITHOUT ORAL OR IV CONTRAST: NO EVIDENCE OF ACUTE INTRA-ABDOMINAL PROCESS; DIVERTICULOSIS WITHOUT EVIDENCE OF DIVERTICULITIS; SUBCUTANEOUS STRANDING ALONG THE ANTERIOR ABDOMINAL WALL GREATEST ON THE RIGHT WHICH MAY BE RELATED TOSCARRING OR EDEMA; POSSIBILITY OF CELLULITIS IS NOT EXCLUDED.; EKG: SINUS TACHYCARDIA; X-RAY CHEST 1 VIEW: THE LUNGS ARE HYPEREXPANDED; PULMONARY VASCULARITY IS PROMINENT; THERE IS AN ENLARGED CARDIOMEDIASTINAL SILHOUETTE; OSSEOUS STRUCTURES ARE WITHIN EXPECTED LIMITS FOR PATIENT'S AGE. CARDIOMEGALY WITHPROMINENCE OF PULMONARY VASCULARITY; PLEASE CORRELATE FOR EARLY CHF.; [redacted]20[redacted] (RX DAY 178): ESOPHAGOGASTRODUODENOSCOPY WITH BIOPSY: MEDIUM HIATAL HERNIA; EROSIVE GASTRITIS - ONE 5 MM ULCER WITH A CLEAN BASE NOTED IN THE ANTRUM.

| | |
|---|---|
| **AE Stopped Rx Day** | 178 |
| **Duration of AE** | 2 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | BLEEDING ULCERS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

**Event #3: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | DIVERTICULITIS |
| **Preferred term** | 憩室炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 238 (17 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted](RX DAY 238): Hemoglobin: 70 [120 - 155] G/L; NPTST484-OCCULT BLOOD X 1: NEG [NOT REPORTED - NOT REPORTED] UNKNOWN; NPTST487-OVA PARASITE SCREEN: NO OVA, CYST, OR PAR [NOT REPORTED - NOT REPORTED] UNKOWN; NPTST595-SHIGA-LIKE TOXIN ANTIGEN, EIA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNKNOWN; Platelets: 68 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 239): Hemoglobin: 78 [120 - 155] G/L; Hemoglobin: 78 [120 - 155] G/L; NPTST211-CULTURE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNKNOWN; Platelets: 62 [150 - 450] 10^9/L; Platelets: 55 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 240): Hemoglobin: 75 [120 - 155] G/L; Hemoglobin: 70 [120 - 155] G/L; Platelets: 23 [150 - 450] 10^9/L; Platelets: 40 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 241): Hemoglobin: 76 [120 - 155] G/L; Platelets: 25 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 242): Hemoglobin: 78 [120 - 155] G/L; Platelets: 27 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 243): Hemoglobin: 71 [120 - 155] G/L; Platelets: 21 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 244): Hemoglobin: 78 [120 - 155] G/L; Hemoglobin: 76 [120 - 155] G/L; Platelets: 19 [150 - 450] 10^9/L; Platelets: 18 [150 -

450] 10^9/L; [redacted]20[redacted](RX DAY 245): NPTST484-OCCULT BLOOD X 1: POSITIVE [NOT REPORTED - NOT REPORTED] UNKNOWN; [redacted]20[redacted] (RX DAY 246): Hemoglobin: 94 [120 - 155] G/L; NPTST498-PATHOLOGY: ABNORMAL [NOT REPORTED - NOT REPORTED] UNKNOWN; Platelets: 40 [150 - 450] 10^9/L; [redacted]20[redacted](RX DAY 247): Hemoglobin: 87 [120 - 155] G/L; Platelets: 58 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 248): Hemoglobin: 288 [120 - 155] G/L; Platelets: 99 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 249): Hemoglobin: 94 [120 - 155] G/L; Hemoglobin: 96 [120 - 155] G/L; Platelets: 164 [150 - 450] 10^9/L; Platelets: 207 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 250): Hemoglobin: 90 [120 - 155] G/L; Platelets: 241 [150 - 450] 10^9/L

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 238): CT ABDOMEN PELVIS WITHOUT ORAL OR IV CONTRAST: SIGMOID DIVERTICULOSIS WITH EARLY OR MILD CHANGES OF DIVERTICULITIS. NO MASS, FREE FLUID OR ADENOPATHY.; EKG: ACCELERATED JUNCTIONAL RHYTHM, LOW VOLTAGE, EXTREMITY AND PRECORDIAL LEADS, PROBABLE ANTEROSEPTAL INFARCT; X-RAY CHEST 1 VIEW: NO ACUTE RADIOGRAPHIC ABNORMALITIES. NO CHANGE BORDERLINE HEART SIZE COMPARED WITH PRIOR STUDY.; [redacted]20[redacted] (RX DAY 239): BX DUODENAL MASS: CHANGES C/W ACTIVE EROSIVE PEPTIC DUODENOPATHY.; ESOPHAGOGASTRODUODENSCOPY/EGD/EUS: EUS:EXERTION THE PANCREAS FROM THE BODY OF THE STOMACH REVEALED THE 4.8 MM HYPOECHOIC LESION WITH A HYPERECHOIC CENTER IN THE GENU OF THE PANCEAS. MY INTENTION WAS TO FNA THIS HOWEVER PATIENT COULD NOT TOLERATE ANESTHESIA ANY FURTHER AS SUCH THE PROCEDURE HAD TO BE ABORTED. PLEASE NOTE THAT I WAS ALSO UNABLE TO EXAMINE THE HEAD OF THE PANCREAS AND AMPULLA DUE TO THE FACT THE PATIENT COULD NOT TOLERATE THE ANESTHESIA. EGD:OROPHARYNX: LIMITED EXAM OF THE POSTERIOR PHARYNX, VOCAL CORDS AND UES APPEARED NORMAL. GE JUNCTION: NORMAL. ESPHAGUS: NORMAL. STOMACH: GASTRITIS. BIOPSIED.ONE 4 MM ULCER.; STOMACH BX: MILD CHRONIC INACTIVE GASTRITIS. NO HELICOBACTER PYLORI ORGANISMS IDENTIFIED; [redacted]20[redacted] (RX DAY 240): PERIPHERAL SMEAR: PANCYTOPENIA WITH SEVERE MACROCYTIC ANEMIA, SLIGHT NEUTROPHILIC LEFT SHIFT, AND THROMBOCYTOPENIA; [redacted]20[redacted] (RX DAY 246): BONE MARROW ASPIRATION: CHANGES C/W MYELODYSPLASTIC SYNDROME WITH MULTIDINEAGE DYSPLASIA & 3-4% BLASTS. HYPERCELLULAR BONE MARROW (50%) WITH ERYTHROID HYPERPLASIA

| | |
|---|---|
| **AE Stopped Rx Day** | 253 (32 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 16 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | DIVERTICULOSIS |
| **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:** M15-572

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，上部消化管出血の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，2 型糖尿病，局面型乾癬，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は上部消化管出血を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，上部消化管出血は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胃腸出血，トロポニン増加，急性失血性貧血，裂孔ヘルニア，消化性潰瘍疾患及びびらん性胃炎で入院した。被験者は悪心，嘔吐及び下痢の症状を呈していた。被験者は改善し，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者が使用していたナプロキセン及びイブプロフェンが本事象の危険因子であると考えられた。

投与された薬剤は，ピペラシリン・タゾバクタム合剤，塩化ナトリウム 0.9%，スクラルファート，pantoprazole 及び zofran であった。

Causality for UPADACITINIB (Blinded)

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1) Upper gastrointestinal bleeding (10071910) (Upper gastrointestinal haemorrhage (10046274) ) [v.22.1] [10071910]

**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)

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Event of UPPER GI BLEED

**- Investigator:** BLEEDING ULCERS

**- AbbVie:** RISK FACTORS INCLUDE SUBJECT'S LONG TERM USE OF NAPROXEN and methotrexate.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] A/G RATIO:** 1.0 ratio (normal 1.5 to 2.5)

[redacted] **20[redacted] ALBUMIN:** 3.1 G/DL (normal 3.6 to 5.1)

[redacted] **20[redacted] BNP:** 155 PG/ML (normal 0 to 100)

[redacted] **20[redacted] BUN:** 47 mg/dL (normal 6.0 to 24)

[redacted] **20[redacted] BUN:** 40 mg/dL

[redacted] **20[redacted] BUN:** 37.0 mg/dL

[redacted] **20[redacted] CREATININE:** 1.5 mg/dL (normal 0.5 to 1.0)

[redacted] **20[redacted] CREATININE:** 1.7 mg/dL (normal 0.5 to 1.0)

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** NO EVIDENCE OF ACUTE INTRA-ABDOMINAL PROCESS; DIVERTICULOSIS WITHOUT EVIDENCE OF DIVERTICULITIS; SUBCUTANEOUS STRANDING ALONG THE ANTERIOR ABDOMINAL WALL GREATEST ON THE RIGHT WHICH MAY BE RELATED TO SCARRING OR EDEMA; POSSIBILITY OF CELLULITIS IS NOT EXCLUDED.

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** NO EVIDENCE OF ACUTE INTRA-ABDOMINAL PROCESS; DIVERTICULOSIS WITHOUT EVIDENCE OF DIVERTICULITIS; SUBCUTANEOUS STRANDING ALONG THE ANTERIOR ABDOMINAL WALL GREATEST ON THE RIGHT WHICH MAY BE RELATED TO SCARRING OR EDEMA; POSSIBILITY OF CELLULITIS IS NOT EXCLUDED.

[redacted] **20[redacted] EGD WITH BIOPSY:** MEDIUM HIATAL HERNIA; EROSIVE GASTRITIS - ONE 5 MM ULCER WITH A CLEAN BASE NOTED IN THE ANTRUM.

[redacted] **20[redacted] EGD WITH BIOPSY:** MEDIUM HIATAL HERNIA; EROSIVE GASTRITIS - ONE 5 MM ULCER WITH A CLEAN BASE NOTED IN THE ANTRUM.

[redacted] **20[redacted] EKG:** SINUS TACHYCARDIA

[redacted] **20[redacted] FECAL OCCULT BLOOD:** Positive

[redacted] **20[redacted] HEMATOCRIT:** 23.7 % (normal 34.9 to 44.5)

[redacted] **20[redacted] HEMATOCRIT:** 25.8 % (normal 34.9 to 44.5)

[redacted] **20[redacted] HEMATOCRIT:** 24.6 % (normal 34.9 to 44.5)

[redacted] **20[redacted] HEMATOCRIT:** 24.1 % (normal 34.9 to 44.5)

[redacted] **20**[redacted] **HEMOGLOBIN:** 7.7 G/DL (normal 12 to 15.5)

[redacted] **20**[redacted] **HEMOGLOBIN:** 8.3 G/DL (normal 12 to 15.5)

[redacted] **20**[redacted] **HEMOGLOBIN:** 8.3 G/DL (normal 12 to 15.5)

[redacted] **20**[redacted] **HEMOGLOBIN:** 7.9 G/DL (normal 12 to 15.5)

[redacted] **20**[redacted] **LACTIC ACID:** 3.1 MMOL/L (normal 0 to 2)

[redacted] **20**[redacted] **MCHC:** 32.8 G/DL (normal 33.4 to 35.5)

[redacted] **20**[redacted] **NEUTROPHILS ABS:** 10.3 X10**3/MCL (normal 1.7 to 7.0)

[redacted] **20**[redacted] **PATHOLOGY:** Stomach biopsy: active erosive gastritis, no helicobacter pylori organisms identified

[redacted] **20**[redacted] **PROTIME:** 12.7 SEC (normal 9.5 to 12.5)

[redacted] **20**[redacted] **RBC:** 2.36 X10**6/MCL (normal 3.9 to 5.03)

[redacted] **20**[redacted] **RBC:** 2.52 X10**6/MCL (normal 3.9 to 5.03)

[redacted] **20**[redacted] **RBC:** 2.47 X10**6/MCL (normal 3.9 to 5.03)

[redacted] **20**[redacted] **RDW:** 17.3 % (normal 11.8 to 15.6)

[redacted] **20**[redacted] **TOTAL PROTEIN:** 6.2 G/DL (normal 6.4 to 8.4)

[redacted] **20**[redacted] **TROPONIN I:** 0.05 NG/ML (normal 0 to 0.04)

[redacted] **20**[redacted] **WBC:** 13.4 X10**3/MCL (normal 4.8 to 10.8)

[redacted] **20**[redacted] **WBC:** 10.9 X10**3/MCL (normal 4.8 to 10.8)

[redacted] **20**[redacted] **X-RAY CHEST:** THE LUNGS ARE HYPEREXPANDED; PULMONARY VASCULARITY IS PROMINENT; THERE IS AN ENLARGED CARDIOMEDIASTINAL SILHOUETTE; OSSEOUS STRUCTURES ARE WITHIN EXPECTED LIMITS FOR PATIENT'S AGE. CARDIOMEGALY WITH PROMINENCE OF PULMONARY VASCULARITY; PLEASE CORRELATE FOR EARLY CHF.
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，憩室炎の事象を発現した。

**Event 3 の臨床経過：**

関連する病歴は，高血圧，2 型糖尿病，糖尿病性ニューロパチー，胃腸出血，甲状腺機能低下症，局面型乾癬，乾癬性関節炎，CKE-STAGE 3，非喫煙者，非飲酒者及び貧血であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

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，憩室炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は重篤な事象である上部消化管出血を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は救急科を受診し，疲労，直腸出血及び吐血を訴えた。被験者はその後入院した。RBC 輸血及び血小板アフェレーシス輸血が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師によると，過去の上部消化管出血が危険因子であると考えられた。

投与された薬剤は，pantoprazole，塩化ナトリウム，シプロフロキサシン，メトロニダゾール，zofran，アセトアミノフェン・コデイン合剤及びピペラシリン・タゾバクタム合剤であった。

**The patient's past medications include:**

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

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

CIPRO for URINARY TRACT INFECTION ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

NITROFURANTOIN for URINARY TRACT INFECTION ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Diverticulitis (10013538) (Diverticulitis (10013538) ) [v.22.1] [10013538]

**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)

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Event of DIVERTICULITIS

**- Investigator:** Diverticulosis

**- AbbVie:** EVENT IS MORE LIKELY RELATED TO SUBJECT'S AGE AND MORBID OBESITY .

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] BIOPSY:** Positive SMALL INTESTINE 'DUODENAL MASS' ENDOSCOPIC BIOPSY: CHANGES C/W ACTIVE EROSIVE PEPTIC DUODENOPATHY. STOMACH, ANTRUM AND BODY, ENDOSCOPIC BIOPSIES: MILD CHRONIC INACTIVE GASTRITIS, NO H.PYLORI ORGANISMS IDENTIFIED

[redacted] **20[redacted] BIOPSY STOMACH:** MILD CHRONIC INACTIVE GASTRITIS. NO HELICOBACTER PYLORI ORGANISMS IDENTIFIED

[redacted] **20[redacted] BONE MARROW ASPIRATION:** CHANGES CONSISTENT WITH MYELODYSPLASTIC SYNDROME WITH MULTIDINEAGE DYSPLASIA & 3-4% BLASTS. HYPERCELLULAR BONE MARROW (50%) WITH ERYTHROID HYPERPLASIA (abnormal)

[redacted] **20[redacted] CHEST X-RAY:** Mild cardiomegaly

[redacted] **20[redacted] CT ABDOMEN PELVIS WITHOUT ORAL OR IV CONTRAST:** SIGMOID DIVERTICULOSIS WITH EARLY OR MILD CHANGES OF DIVERTICULITIS. NO MASS, FREE FLUID OR ADENOPATHY

[redacted] **20[redacted] DUODENAL MASS BIOPSY:** CHANGES CONSISTENT WITH ACTIVE EROSIVE PEPTIC DUODENOPATHY.

[redacted] **20[redacted] EKG:** ACCELERATED JUNCTIONAL RHYTHM, LOW VOLTAGE, EXTREMITY AND PRECORDIAL LEADS, PROBABLE ANTEROSEPTAL INFARCT

[redacted] **20[redacted] ESOPHAGOGASTRODUODENOSCOPY:** EUS: EXERTION THE PANCREAS FROM THE BODY OF THE STOMACH REVEALED THE 4.8 MM HYPOECHOIC LESION WITH A HYPERECHOIC CENTER IN THE GENU OF THE PANCEAS. MY INTENTION WAS TO FNA THIS, HOWEVER, PATIENT COULD NOT TOLERATE ANESTHESIA ANY FURTHER AS SUCH THE PROCEDURE HAD TO BE ABORTED. PLEASE NOTE THAT I WAS ALSO UNABLE TO EXAMINE THE HEAD OF THE PANCREAS AND AMPULLA DUE TO THE FACT THE PATIENT COULD NOT TOLERATE THE ANESTHESIA. EGD:OROPHARYNX: LIMITED EXAM OF THE POSTERIOR PHARYNX, VOCAL CORDS AND UES APPEARED NORMAL. GE JUNCTION: NORMAL. ESPHAGUS: NORMAL. STOMACH: GASTRITIS. BIOPSIED.ONE 4 MM ULCER.

[redacted] 20[redacted] **HEMOGLOBIN:** 7.0 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 7.8 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 7.0 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 7.5 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 7.6 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 7.8 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 7.1 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 7.6 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 7.8 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 8.7 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 28.8 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.4 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.0 G/DL (normal 12.0 to 15.50)

[redacted] 20[redacted] **NOSE CULTURE:** Negative

[redacted] 20[redacted] **OCCULT BLOOD:** Negative

[redacted] 20[redacted] **OCCULT BLOOD:** Positive

[redacted] 20[redacted] **PERIPHERAL SMEAR:** PANCYTOPENIA WITH SEVERE MACROCYTIC ANEMIA, SLIGHT NEUTROPHILIC LEFT SHIFT, AND THROMBOCYTOPENIA

[redacted] 20[redacted] **PLATELET COUNT:** 60 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 62 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 40 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 24 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 21 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 25 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 27 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 19 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 18 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 40 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 58 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 99 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 164 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 207 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 241 10^3/uL (normal 150 to 450)

[redacted] 20[redacted] **SHIGA-LIKE TOXIN ANTIGEN, EIA FROM STOOL SAMPLE:** Negative

[redacted] 20[redacted] **X-RAY CHEST 1 VIEW:** NO ACUTE RADIOGRAPHIC ABNORMALITIES. NO CHANGE BORDERLINE HEART SIZE COMPARED WITH PRIOR STUDY

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 |
|---|---|---|---|---|
| 頚部脊柱管狭窄症 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 15 mg QD | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: C4 C5 FUSION | 20[redacted] |
| OTHER: CERVICAL SPONDYLOSIS WITH MYELOPATHY | 20 |
| OTHER: VASOVAGAL SYNCOPE | 20 |
| OBESITY | 20 |
| OTHER: PERIPHERAL VASCULAR DISEASE BILATERAL FEET | 20 |
| OTHER: THYROTOXICOSIS | 20 |
| OTHER: DYSPEPSIA | 20 |
| DEPRESSION | 20 |
| OTHER: ANXIETY | 20 |
| OTHER: INSOMNIA | 20 |
| OTHER: ELEVATION OF LDH LEVELS | 20 |
| OTHER: NONSPECIFIC MILD ELEVATION OF TRANSAMINASE | 20 |
| OTHER: PLAQUE PSORIASIS | 20 |
| HYPERTENSION | 20 |
| OTHER: IRRITABLE BOWEL SYNDROME | 20 |
| OTHER: EXERCISE INDUCED ASTHMA | 20 |
| OTHER: LEFT HIP REPLACEMENT | 20 |
| PSORIATIC ARTHRITIS | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: LEFT ULNAR TRANSPOSITION SURGERY | 20[redacted] |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted] / 1 | [redacted] / 168 | 168 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 169 | [redacted] / 390 | 222 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 391 | [redacted] / 1069 | 679 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| OMEPRAZOLE | 40 mg | QD | Y-M: 20[redacted] |
| ESCITALOPRAM | 10 mg | QD | Y-M: 20[redacted] |
| VENLAFAXINE | 75 mg | QD | Y-M: 20[redacted] |
| BUSPIRONE | 20 mg | QD | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] |
| LOSARTAN | 100 mg | QD | Y-M: 20[redacted] |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] / -216 |
| SALBUTAMOL | 90 OTHER: MCG | PRN | Y-M: 20[redacted] / -216 |
| PREDNISONE | 20 mg | QD | Y-M: 20[redacted] / -210 |
| CELECOXIB | 200 mg | BID | Y-M: 20[redacted] / -169 |
| ESOMEPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / -169 |
| LORAZEPAM | 0.5 mg | QD | Y-M: 20[redacted] / -169 |
| VALPROIC ACID | 250 mg | QD | Y-M: 20[redacted] / -169 |
| VENLAFAXINE | 75 mg | QD | Y-M: 20[redacted] / -169 |
| FOLIC ACID | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -160 |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] / -160 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -132 |

**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 |
|---|---|---|---|---|
| ESCITALOPRAM | 10 mg | QD | Y-M: 20[redacted] | ONGOING |
| BUSPIRONE | 20 mg | QD | Y-M: 20[redacted] | ONGOING |
| LOSARTAN | 100 mg | QD | Y-M: 20[redacted] | ONGOING |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] / -216 | ONGOING |
| SALBUTAMOL | 90 OTHER: MCG | PRN | Y-M: 20[redacted] / -216 | ONGOING |
| CELECOXIB | 200 mg | BID | Y-M: 20[redacted] / -169 | ONGOING |
| ESOMEPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / -169 | ONGOING |
| LORAZEPAM | 0.5 mg | QD | Y-M: 20[redacted] / -169 | ONGOING |
| VALPROIC ACID | 250 mg | QD | Y-M: 20[redacted] / -169 | ONGOING |
| VENLAFAXINE | 75 mg | QD | Y-M: 20[redacted] / -169 | ONGOING |
| FOLIC ACID | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -160 | ONGOING |
| METHOTREXATE | 7.5 mg | EVERY WEEK | Y-M: 20[redacted] / 260 | ONGOING |
| BUPIVACAINE | 0.25 % | OTHER: ONCE | Y-M: 20[redacted] / 318 | Y-M: 20[redacted] / 318 |
| EPINEPHRINE | 30 mL | OTHER: ONCE | Y-M: 20[redacted] / 318 | Y-M: 20[redacted] / 318 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | CERVICAL STENOSIS |
| **Preferred term** | 頚部脊柱管狭窄症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 318 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**
NOT REPORTED
**Microbiology**
NOT REPORTED
**SAE Supplemental Procedure**
[redacted]20[redacted] (RX DAY 318): C3, C4, C5, C6, C7 POSTERIOR LAMINECTOMIES: EXTUBATED, AWAKE, AND STABLE TO THE RECOVERY ROOM IN GOOD CONDITION

| | |
|---|---|
| **AE Stopped Rx Day** | 321 |
| **Duration of AE** | 4 DAYS |
| **Severity** | Mild |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | CERVICAL SPONDYLOSIS WITH MYELOPATHY |
| **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:** M15-572

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，頚椎狭窄の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，C4 及び C5 の融合，頚椎症性脊髄症，肥満，甲状腺中毒症，左尺骨転位術，局面型乾癬，左人工股関節置換術，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は頚椎狭窄を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，頚椎狭窄は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，頚椎狭窄に続発した神経根障害に伴う薬剤抵抗性頚部痛のため入院した。同日，被験者は，頚椎狭窄治療並びに頚椎・神経根除圧のための C3，C4，C5，C6 及び C7 の後方椎弓切除術を受けた。治療の一環として理学療法が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for UPADACITINIB (Blinded)

---

1) Spinal stenosis cervical (10041593) (Cervical spinal stenosis (10008313) ) [v.23.0] [10041593]

**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 CERVICAL STENOSIS

**- Investigator:** CERVICAL SPONDYLOSIS WITH MYELOPATHY

**- AbbVie:** Event more likely related to pre-existing cervical spondylosis with myelopathy and prior C4-C5 fusion [redacted] 20[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 |
|---|---|---|---|---|
| コロナウイルス感染 | X | X | X | X |
| 肺炎 | X | | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 30 mg QD | 4[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ASTHMA | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20 |
| OBESITY | 20 |
| OTHER: PARESTHESIA OF SKIN | 20 |
| OTHER: SACROILITIS | 20 |
| PSORIATIC ARTHRITIS | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: LEFT KNEE ARTHROSCOPY | 19[redacted] |
| SURGERY: LEFT KNEE MENISCAL SURGERY | 19 |
| SURGERY: CHOLECYSTECTOMY | 20 |
| SURGERY: HERNIA REPAIR | 20 |
| SURGERY: LEFT SHOULDER ARTHROSCOPY | 20 |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted] / 1 | [redacted] / 168 | 168 |
| ABT-494 | 30 MG | ORAL | QD | [redacted] / 169 | [redacted] / 389 | 221 |
| ABT-494 | 30 MG | ORAL | QD | [redacted] / 390 | [redacted] / 956 | 567 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| RANITIDINE | 300 mg | QD | Y-M: 20[redacted] |
| SALBUTAMOL | 50 OTHER: MCG | PRN | Y-M: 20[redacted] |
| SERETIDE | 50 OTHER: MCG | PRN | Y-M: 20[redacted] |
| FLUOCINONIDE | 0.1 % | QD | Y-M: 20[redacted] / -208 |
| IBUPROFEN | 800 mg | TID | Y-M: 20[redacted] / -138 |
| FOLIC ACID | 1 OTHER: TAB | QD | Y-M: 20[redacted] / -117 |
| HYDROCODONE | 325 mg | QD | Y-M: 20[redacted] / -117 |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] / -117 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -88 |

**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 |
|---|---|---|---|---|
| RANITIDINE | 300 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 975 |
| SALBUTAMOL | 50 OTHER: MCG | PRN | Y-M: 20[redacted] | Y-M: 20[redacted] / 975 |
| SERETIDE | 50 OTHER: MCG | PRN | Y-M: 20[redacted] | Y-M: 20[redacted] / 975 |
| IBUPROFEN | 800 mg | TID | Y-M: 20[redacted] / -138 | Y-M: 20[redacted] / 975 |
| FOLIC ACID | 1 OTHER: TAB | QD | Y-M: 20[redacted] / -117 | Y-M: 20[redacted] / 975 |
| HYDROCODONE | 325 mg | QD | Y-M: 20[redacted] / -117 | Y-M: 20[redacted] / 975 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -88 | Y-M: 20[redacted] / 975 |
| AMLODIPINE | 2.5 mg | QD | Y-M: 20[redacted] / 242 | Y-M: 20[redacted] / 975 |
| BUDESONIDE | 0.5 mg | OTHER: ONCE | Y-M: 20[redacted] / 956 | Y-M: 20[redacted] / 956 |
| CEFTRIAXONE | 1 g | OTHER: ONCE | Y-M: 20[redacted] / 956 | Y-M: 20[redacted] / 956 |
| LEVOSALBUTAMOL | 1.25 mg | BID | Y-M: 20[redacted] / 956 | Y-M: 20[redacted] / 956 |
| LEVOSALBUTAMOL | 1.25 mg | OTHER: ONCE | Y-M: 20[redacted] / 956 | Y-M: 20[redacted] / 956 |
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted] / 956 | Y-M: 20[redacted] / 956 |
| AZITHROMYCIN | 500 mg | QD | Y-M: 20[redacted] / 956 | Y-M: 20[redacted] / 975 |
| HYDROXYCHLOROQUINE | 400 mg | QD | Y-M: 20[redacted] / 956 | Y-M: 20[redacted] / 975 |
| TOCILIZUMAB | 800 mg | OTHER: ONCE | Y-M: 20[redacted] / 958 | Y-M: 20[redacted] / 958 |

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

**Event Description** COVID-19 INFECTION
**Preferred term** コロナウイルス感染
**AE Onset Date / Rx Day** [redacted] / 956

| | |
|---|---|
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 956): Albumin: 40 [34 - 54] G/L; Bilirubin: 1 [0 - 1] UMOL/L; Chloride: 97 [96 - 106] MMOL/L; Creatinine: 97 [53 - 106] UMOL/L; Erythrocytes: 4 [3.6 - 4.9] 10^12/L; Glucose: 7.2 [7.8 - 11.1] MMOL/L; Hematocrit: 0.37 [0.31 - 0.42] FRACTION OF 1; Hemoglobin: 126 [109 - 143] G/L; Leukocytes: 16.3 [3.8 - 11.8] 10^9/L; NPTST604-SODIUM LVL: 137 [136 - 145] MMOL/L; Potassium: 2.8 [3.6 - 5.2] MMOL/L; Protein: 79 [60 - 83] G/L; [redacted]20[redacted] (RX DAY 972): NPTST177-CO2 ART: 40 [35 - 45] 099,MMHG; NPTST314-HC03 ART: 29 [22 - 26] MMOL/L; NPTST509-PH ART: 7.48 [7.35 - 7.45] 099,MMHG; NPTST519-PO2 ART: 55 [83 - 108] 099,MMHG

**Microbiology**

[redacted]20[redacted] (RX DAY 956): BLOOD NPTST097-BETA-D-GLUCAN: Not applicable-56 PG/ML; BLOOD NPTST384-INFLUENZA A, PCR: Negative-NOT DETECTED; BLOOD NPTST388-INFLUENZA B, PCR: Negative-NOT DETECTED; BLOOD NPTST553-QUANTIFERON-TB PLUS 1T: Not applicable-INDETERMINATE; SPUTUM NPTST582-RSV PCR: Negative-NOT DETECTED; [redacted]20[redacted] (RX DAY 957): OTHER NASOPHARYNGEAL NPTST197-COVID-19 RNA: Positive-RESULT - DETECTED; [redacted]20[redacted] (RX DAY 959): STOOL NPTST145-CARBAPENEM RESISTANCE SCREEN RE: Negative-NO CARBAPENEM-RESISTANT ENTEROBACTERIACEAE ISOLATED.; SPUTUM NPTST457-MRSA SURVEILLANCE CULTURE: Negative-NO METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) ISOLATED; SPUTUM NPTST608-SPUTUM CULTURE WITH GRAM STAIN: Positive-LIGHT GROWTH CANDIDA ALBICANS.; [redacted]20[redacted] (RX DAY 967): BLOOD NPTST354-HSV-1: Positive-DETECTED; [redacted]20[redacted] (RX DAY 974): URINE NPTST144-CANDIDA ALBICANS: Negative-NO GROWTH AT 5 DAYS

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 957): CT OF THE CHEST WITHOUT CONTRAST.: FINDINGS CONSISTENT WITH BILATERAL PNEUMONIA. IN FURTHER DETAIL AND SUSPICIOUS FOR COVID-19 PNEUMONIA. MARGINAL MIDDLE MEDIASTINAL ADENOPATHY.; CT THORAX W/O CONTRAST: SUSPICIOUS FOR COVID-19 PNEUMONIA; X-RAY PORTABLE CHEST 1 VIEW: BETTER AERATION WITH NEAR COMPLETELY RESOLVED ATELECTASIS/INTERSTITIAL INFILTRATES.; [redacted]20[redacted] (RX DAY 958): X-RAY PORTABLE CHEST 1 VIEW: MODERATELY WELL-EXPANDED LUNGS. MULTIFOCAL PATCHY OPACITIES WHICH APPEAR WORSENED. BIBASILAR ATELECTASIS. SMALL LEFT PLEURAL EFFUSION SUSPECTED.; [redacted]20[redacted] (RX DAY 959): ENDOTRACHEAL TUBE: N/A; PORT ABD-NG CATHERTER PLACEMENT: NASOGASTRIC TUBE DEMONSTRATED WITH DISTAL PORTION IN STOMACH AND TIP IN REGION OF THE GASTRIC BODY. NONSPECIFIC BOWEL GAS PATTERN.; X-RAY PORTABLE CHEST: ENDOTRACHEAL TUBE IN GOOD POSITION. INCREASE IN ASYMMETRIC INTERSTITIAL INFILTRATES.; [redacted]20[redacted] (RX DAY 961): X-RAY PORTABLE CHEST 1 VIEW: MINIMAL CHANGE IN THE INTERSTITIAL EDEMA VERSUS PNEUMONIA.; [redacted]20[redacted] (RX DAY 963): X-RAY OF PORTABLE CHEST 1 VIEW: MINIMAL CHANGE IN THE INTERSTITIAL EDEMA VERSUS PNEUMONIA.; [redacted]20[redacted] (RX DAY 968): X-RAY PORTABLE CHEST 1 VIEW: THERE IS PERSISTENT MODERATE DIFFUSE BILATERAL PULMONARY INFILTRATES THAT SLIGHTLY PROGRESSIVE ON THE RIGHT.; [redacted]20[redacted] (RX DAY 970): X-RAY PORTABLE CHEST 1 VIEW: MILD PROGRESSION OF SEVERE DIFFUSE BILATERAL PULMONARY INFILTRATES.; [redacted]20[redacted] (RX DAY 973): X-RAY OF CHEST 1 VIEW: BILATERAL INFILTRATES.

| | |
|---|---|
| **AE Stopped Rx Day** | 975 (19 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 20 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION, PERSIST OR SIGNIF DISABILITY/INCAPACITY, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING, RESULTS IN DEATH |

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

| | |
|---|---|
| **Event Description** | PNEUMONIA |

| | |
|---|---|
| **Preferred term** | 肺炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 956 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 956): Albumin: 40 [34 - 54] G/L; Bilirubin: 1 [0 - 1] UMOL/L; Chloride: 97 [96 - 106] MMOL/L; Creatinine: 97 [53 - 106] UMOL/L; Erythrocytes: 4 [3.6 - 4.9] 10^12/L; Glucose: 7.2 [7.8 - 11.1] MMOL/L; Hematocrit: 0.37 [0.31 - 0.42] FRACTION OF 1; Hemoglobin: 126 [109 - 143] G/L; Leukocytes: 16.3 [3.8 - 11.8] 10^9/L; NPTST604-SODIUM LVL: 137 [136 - 145] MMOL/L; Potassium: 2.8 [3.6 - 5.2] MMOL/L; Protein: 79 [60 - 83] G/L; [redacted]20[redacted] (RX DAY 972): NPTST177-CO2 ART: 40 [35 - 45] 099,MMHG; NPTST314-HC03 ART: 29 [22 - 26] MMOL/L; NPTST509-PH ART: 7.48 [7.35 - 7.45] 099,MMHG; NPTST519-PO2 ART: 55 [83 - 108] 099,MMHG

**Microbiology**

[redacted]20[redacted] (RX DAY 956): BLOOD NPTST097-BETA-D-GLUCAN: Not applicable-56 PG/ML; BLOOD NPTST384-INFLUENZA A, PCR: Negative-NOT DETECTED; BLOOD NPTST388-INFLUENZA B, PCR: Negative-NOT DETECTED; BLOOD NPTST553-QUANTIFERON-TB PLUS 1T: Not applicable-INDETERMINATE; SPUTUM NPTST582-RSV PCR: Negative-NOT DETECTED; [redacted]20[redacted] (RX DAY 957): OTHER NASOPHARYNGEAL NPTST197-COVID-19 RNA: Positive-RESULT - DETECTED; [redacted]20[redacted] (RX DAY 959): STOOL NPTST145-CARBAPENEM RESISTANCE SCREEN RE: Negative-NO CARBAPENEM-RESISTANT ENTEROBACTERIACEAE ISOLATED.; SPUTUM NPTST457-MRSA SURVEILLANCE CULTURE: Negative-NO METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) ISOLATED; SPUTUM NPTST608-SPUTUM CULTURE WITH GRAM STAIN: Positive-LIGHT GROWTH CANDIDA ALBICANS.; [redacted]20[redacted] (RX DAY 967): BLOOD NPTST354-HSV-1: Positive-DETECTED; [redacted]20[redacted] (RX DAY 974): URINE NPTST144-CANDIDA ALBICANS: Negative-NO GROWTH AT 5 DAYS

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 957): CT OF THE CHEST WITHOUT CONTRAST.: FINDINGS CONSISTENT WITH BILATERAL PNEUMONIA. IN FURTHER DETAIL AND SUSPICIOUS FOR COVID-19 PNEUMONIA. MARGINAL MIDDLE MEDIASTINAL ADENOPATHY.; CT THORAX W/O CONTRAST: SUSPICIOUS FOR COVID-19 PNEUMONIA; X-RAY PORTABLE CHEST 1 VIEW: BETTER AERATION WITH NEAR COMPLETELY RESOLVED ATELECTASIS/INTERSTITIAL INFILTRATES.; [redacted]20[redacted] (RX DAY 958): X-RAY PORTABLE CHEST 1 VIEW: MODERATELY WELL-EXPANDED LUNGS. MULTIFOCAL PATCHY OPACITIES WHICH APPEAR WORSENED. BIBASILAR ATELECTASIS. SMALL LEFT PLEURAL EFFUSION SUSPECTED.; [redacted]20[redacted] (RX DAY 959): ENDOTRACHEAL TUBE: N/A; PORT ABD-NG CATHERTER PLACEMENT: NASOGASTRIC TUBE DEMONSTRATED WITH DISTAL PORTION IN STOMACH AND TIP IN REGION OF THE GASTRIC BODY. NONSPECIFIC BOWEL GAS PATTERN.; X-RAY PORTABLE CHEST: ENDOTRACHEAL TUBE IN GOOD POSITION. INCREASE IN ASYMMETRIC INTERSTITIAL INFILTRATES.; [redacted]20[redacted] (RX DAY 961): X-RAY PORTABLE CHEST 1 VIEW: MINIMAL CHANGE IN THE INTERSTITIAL EDEMA VERSUS PNEUMONIA.; [redacted]20[redacted] (RX DAY 963): X-RAY OF PORTABLE CHEST 1 VIEW: MINIMAL CHANGE IN THE INTERSTITIAL EDEMA VERSUS PNEUMONIA.; [redacted]20[redacted] (RX DAY 968): X-RAY PORTABLE CHEST 1 VIEW: THERE IS PERSISTENT MODERATE DIFFUSE BILATERAL PULMONARY INFILTRATES THAT SLIGHTLY PROGRESSIVE ON THE RIGHT.; [redacted]20[redacted](RX DAY 970): X-RAY PORTABLE CHEST 1 VIEW: MILD PROGRESSION OF SEVERE DIFFUSE BILATERAL PULMONARY INFILTRATES.; [redacted]20[redacted] (RX DAY 973): X-RAY OF CHEST 1 VIEW: BILATERAL INFILTRATES.

| | |
|---|---|
| **AE Stopped Rx Day** | 975 (19 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 20 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION, PERSIST OR SIGNIF DISABILITY/INCAPACITY, LIFE THREATENING |

Generated: [redacted]

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，致死的な新型コロナウイルス感染症及び肺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，喘息，局面型乾癬，肥満，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は新型コロナウイルス感染症及び肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死因は新型コロナウイルス感染症と報告された。剖検は実施されなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し ICU に入室した。入院時，発熱，咽喉痛，咳嗽，呼吸困難及び低酸素症の症状が認められた。被験者は PCP 肺炎の治療を受け，新型コロナウイルス陽性と判明した。被験者は挿管され，治療後も挿管されたままであった。同日，NG チューブが挿入された。被験者は感染症科の診察を受け，治療が行われた。15 日間の治療終了後，被験者に改善は認められず，きわめて予後不良であった。緩和ケアチームによる診察が行われ，家族は終末期としての抜管に同意した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。

**医療記録より：**

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 103°F の発熱を来した。被験者によると，それ以降発熱と解熱を繰り返し，次第に呼吸困難が悪化し，緑色痰を伴う咳嗽及び咽喉痛が見られた。被験者は救急診療所（urgent care）を受診しアモキシシリンを処方された。20[redacted] 年 [redacted] 月 [redacted] 日に病院に搬送されたときには，酸素飽和度を 90%台に保つため非再呼吸式マスクが必要であった。被験者は BiPAP を装着された。その時点で挿管が提案されたが，被験者は拒否した。被験者によると，病人との接触はなかった。同居家族は夫と子ども 4 人であったが，誰も病気ではなかったという。また，旅行もしていなかった。2 週間前に回復期患者向け施設にいる父親を訪ねていたが，父親は病気

ではなく，その時点でその場でほかの病人には気付かなかったとのことであった。

被験者はICUに入室し，経験的治療に基づく抗生物質投与と気管支拡張薬投与が開始された。HSV-1 の可能性から，アシクロビルの投与も開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は挿管され，昇圧薬の投与が必要となった。20[redacted] 年 [redacted] 月 [redacted] 日，NG チューブが留置された。被験者はそれ以上の治療を拒否し続け，皮膚に浮腫と水疱が出現した。入院中，腎臓内科の診察を受け，急性腎不全に対しヘパリン療法が開始された。急性腎不全は新型コロナウイルスの合併症である塞栓症が原因である可能性が高いと考えられた。被験者は改善せず，予後不良であった。医師は患者の状態を家族と話し合い，家族は患者の状態を「蘇生処置拒否」に変更することを決定した。被験者はその時点で 100%の酸素が必要な状態であった。

投与された薬剤は，メトロニダゾール，トシリズマブ，アシクロビル，ヒドロキシクロロキン，xopenex，パルミコート，cefipime，bactrim，solumedrol，プラケニル，zithromax 及び dextrose 10%であった。

**The patient's past medications include:**

FLUOCINONIDE for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) COVID-19 (10084268) (COVID-19 (10084268) ) [v.23.0] [10084268]

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

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

**Dechallenge:** Not Applicable

2) Pneumonia (10035664) (Pneumonia (10035664) ) [v.23.0] [10035664]

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

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

**Dechallenge:** Unknown

Alternative Etiology for UPADACITINIB (Blinded)

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Event of COVID-19 INFECTION

**- Investigator:** Not applicable.

**- AbbVie:** Event is more likely related to a pandemic outbreak that has spread worldwide.

Event of PNEUMONIA

**- Investigator:** Not applicable.

**- AbbVie:** Event is more likely a complication from concomitant COVID-19 infection.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ARTERIAL CO2:** 60 mmHg

[redacted] **20[redacted] ARTERIAL PH:** 7.38 no unit

[redacted] **20[redacted] ARTERIAL PO2:** 107 mmHg

[redacted] **20[redacted] ARTERIAL SPO2:** 94 %

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

[redacted] **20[redacted] BMI:** 48.6 kg/m*2

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

[redacted] **20[redacted] BODY TEMPERATURE:** 37.9 Degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** 37.0 Degrees C

[redacted] **20[redacted] BODY WEIGHT:** 249 Pounds

[redacted] **20[redacted] BODY WEIGHT:** 103.4 KG

[redacted] **20[redacted] BODY WEIGHT:** 108.6 KG

[redacted] **20[redacted] BODY WEIGHT:** 109.1 KG

[redacted] **20[redacted] BUN:** 29 mg/dL

[redacted] **20[redacted] BUN:** 26 mg/dL

[redacted] 20[redacted] **CARBAPENEM RESISTANCE SCREEN RECTAL:** No carbapenem-resistant enterobaceriaceae isolated

[redacted] 20[redacted] **CHEST X-RAY:** Bilateral infiltrates, slightly improved.

[redacted] 20[redacted] **COVID-19 RNA:** Positive-detected

[redacted] 20[redacted] **CREATININE:** 1.1 mg/dL

[redacted] 20[redacted] **CREATININE:** 0.6 mg/dL

[redacted] 20[redacted] **CRP:** 13.5 mg/dL

[redacted] 20[redacted] **CT THORAX:** Findings consistent with bilateral pneumonia. In further detail and suspicious for COVID-19 pneumonia. Marginal middle mediastinal adenopathy.

[redacted] 20[redacted] **FIO2 ARTERIAL:** 100 %

[redacted] 20[redacted] **HCO3 ARTERIAL:** 35 MMOL/L

[redacted] 20[redacted] **HCT:** 37.3 %

[redacted] 20[redacted] **HCT:** 24.1 %

[redacted] 20[redacted] **HGB:** 12.6 G/DL

[redacted] 20[redacted] **HGB:** 7.9 G/DL

[redacted] 20[redacted] **INFLUENZA A TEST:** Negative

[redacted] 20[redacted] **INFLUENZA B TEST:** Negative

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 0.3 X10**3/MCL

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 1.2 X10**3/MCL

[redacted] 20[redacted] **MRSA SURVEILLANCE CULTURE:** No Methicillin resistant Staphylococcus aureus (MRSA) isolated

[redacted] 20[redacted] **NEUTROPHILS ABS:** 8.3 X10**3/MCL

[redacted] 20[redacted] **NEUTROPHILS ABS:** 37.1 X10**3/MCL

[redacted] 20[redacted] **PTT:** 64.2 SEC

[redacted] 20[redacted] **RBC:** 4.04 X10**6/MCL

[redacted] 20[redacted] **RBC:** 2.52 X10**6/MCL

[redacted] 20[redacted] **RESPIRATORY RATE:** 26 /min

[redacted] 20[redacted] **RSV:** Negative

[redacted] 20[redacted] **SPUTUM COLLECTION:** Positive for COVID-19

[redacted] 20[redacted] **SPUTUM CULTURE WITH GRAM STAIN:** light growth candida albicans/dublinensis

[redacted] 20[redacted] **URINALYSIS:** Abnormal: bacteria moderate, WBC 72/HPF, RBC 119/HPF, Yeast: many ins

[redacted] 20[redacted] **VRE SCREEN:** Vancomycin resistant enterococcus isolated

[redacted] 20[redacted] **WBC:** 8.8 X10**3/MCL

[redacted] 20[redacted] **WBC:** 40.8 X10**3/MCL

[redacted] 20[redacted] **X-RAY CHEST:** Moderate left basilar infiltrate. Minimal infiltrate/atelectasis at the right lung base.

[redacted] 20[redacted] **X-RAY CHEST:** Assessment of lung windows demonstrates primarily peripherally located patchy areas of ground glass opacification with more dense consolidation and possibly atelectasis posterior aspects of both lower lobes basilar segment. No evidence of pleural fluid. No pneumothoraces are seen. Findings consistent with bilateral pneumonia as discussed. Suspicious for COVID 19 pneumonia.

[redacted] 20[redacted] **X-RAY CHEST:** Moderately well-expanded lungs. Multifocal patchy opacities which appear worsened. Bibasilar atelectasis. Small left pleural effusion suspected.

[redacted] 20[redacted] **X-RAY CHEST:** Mildly improved inflation lungs, withpersistent pulmonary vascular and/or pneumonitis less likely. Possible small left pleural effusion and or pleural fibrosis.

[redacted] 20[redacted] **X-RAY CHEST:** Minimal change in the interstitial edema versus Pneumonia.

[redacted] 20[redacted] **X-RAY CHEST:** Minimal change in the interstitial edema versus pneumonia.

[redacted] 20[redacted] **X-RAY CHEST:** There is persistent moderate diffuse bilateral pulmonary infiltrates that slightly progressive on the right.

[redacted] 20[redacted] **X-RAY CHEST:** Mild progression of severe diffuse bilateral pulmonary infiltrates.

[redacted] 20[redacted] **X-RAY CHEST:** Bilateral Infilrates

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 |
|---|---|---|---|---|
| 胸痛 | X | X | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 30 mg QD | 7[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: OSTEOARTHRITIS | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| HYPOTHYROIDISM | 20[redacted] |
| OBESITY | 20[redacted] |
| OTHER: DIABETIC NEUROPATHY | 20[redacted] |
| OTHER: HYPERCHOLESTEREMIA | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| DEPRESSION | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| DIABETES MELLITUS | 20[redacted] |
| OTHER: ALLERGIC TO MORPHINE SULFATE | 20[redacted] |
| OTHER: ATRIAL FIBRILLATION | 20[redacted] |
| OTHER: CORONARY ARTERY DISEASE | 20[redacted] |
| MYOCARDIAL INFARCTION | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: HYSTERECTOMY | 19[redacted] |
| SURGERY: STENT RCA | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 5 | 20[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 112 | 112 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ATORVASTATIN | 80 mg | QD | Y-M: 20[redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] |
| GABAPENTIN | 900 mg | BID | Y-M: 20[redacted] |
| IRON | 325 mg | QD | Y-M: 20[redacted] |
| LEVOTHYROXINE | 75 OTHER: MCG | QD | Y-M: 20[redacted] |
| LISINOPRIL | 20 mg | BID | Y-M: 20[redacted] |
| METFORMIN | 850 mg | BID | Y-M: 20[redacted] |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] |
| METOPROLOL | 50 mg | QD | Y-M: 20[redacted] |
| APIXABAN | 5 mg | BID | Y-M: 20[redacted] / -240 |
| CLOPIDOGREL | 75 mg | QD | Y-M: 20[redacted] / -240 |

**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 |
|---|---|---|---|---|
| ATORVASTATIN | 80 mg | QD | Y-M: 20[redacted] | ONGOING |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] | ONGOING |
| GABAPENTIN | 900 mg | BID | Y-M: 20[redacted] | ONGOING |
| IRON | 325 mg | QD | Y-M: 20[redacted] | ONGOING |
| LEVOTHYROXINE | 75 OTHER: MCG | QD | Y-M: 20[redacted] | ONGOING |
| LISINOPRIL | 20 mg | BID | Y-M: 20[redacted] | ONGOING |
| METFORMIN | 850 mg | BID | Y-M: 20[redacted] | ONGOING |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] | ONGOING |
| METOPROLOL | 50 mg | QD | Y-M: 20[redacted] | ONGOING |
| APIXABAN | 5 mg | BID | Y-M: 20[redacted] / -240 | ONGOING |
| CLOPIDOGREL | 75 mg | QD | Y-M: 20[redacted] / -240 | ONGOING |
| GLYCERYL TRINITRATE | 0.4 mg | PRN | Y-M: 20[redacted] / 112 | Y-M: 20[redacted] / 112 |

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

| | |
|---|---|
| **Event Description** | CHEST PAIN |
| **Preferred term** | 胸痛 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 112 |
| **Age at AE Onset** | 7[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 112): Hematocrit: 0.42 [0.33 - 0.44] FRACTION OF 1; Hemoglobin: 139 [110 - 148] G/L; NPTST654-TRP: 0.17 [0 - 0.05] NG/ML; [redacted]20[redacted] (RX DAY 113): NPTST654-TRP: 0.23 [0 - 0.05] NG/ML; NPTST654-TRP: 0.25 [0 - 0.05] NG/ML

**Microbiology**
NOT REPORTED
**SAE Supplemental Procedure**
[redacted]20[redacted] (RX DAY 112): CHEST X RAY: NO ACUTE PULMONARY DISEASE. BORDERLINE CARDIOMEGALY.; ELECTROCARDIOGRAM: A FIB WITH RAPID VENTRICULAR RESPONSE, LEFT AXIS DEVIATION, LBBB.; [redacted]20[redacted] (RX DAY 113): ECHOCARDIOGRAM: NORMAL LEFT VENTRICULAR SYSTOLIC FUNCTION. MODERATE ANNULAR CALCIFICATION. MILD THICKENING OF BOTH LEAFLET OF MITRAL VALVE WITH MILDLY REDUCED MOBILITY. MILDLY INCREASED LEFT ATRIAL SIZE. MODERATE CONCENTRIC LEFT VENTRICULAR HYPERTROPHY. AORTIC SCLEROSIS WITHOUT HEMODYNAMICALLY SIGNIFICANT STENOSIS AND NO SIGNIFICANT INSUFFICIENCY.; ELECTROCARDIOGRAM: NORMAL SINUS RHYTHM, LEFT AXIS DEVIATION, LEFT VENTRICULAR HYPERTROPHY WITH QRS WIDENING AND REPOLARIZATION ABNORMALITY.; INSTANTANEOUS FRACTIONAL FLOW RESERVE OF THE OSTIUM OF THE LEFT ANTERIOR DESCENDING ARTERY.: THE RIGHT CORONARY ARTERY IS A LARGE SIZE VESSEL, DOMINANT. IN THE PROXIMAL SEGMENT, THE STENTS ARE PATENT. DISTALLY, THERE IS NO SIGNIFICANT DISEASE. IT BIFUCRATES INTO A POSTERIOR DESCENDING ARTERYAND POSTEROLATERAL VESSEL WITH NO SIGNIFICANT DISEASE.; INSTANTANEOUS FRACTIONAL FLOW RESERVE OF THE RAMUS INTERMEDIUS: NORMALIZED THE WIRE BEFORE INSERTING THE GUIDE. ENGAGED THE OSTIUM OF THE LEFT ANTERIOR DESCENDING ARTERY. IFR WAS 0.95, INDICATING NONSIGNIFICANT STENOSIS. DID THE SAME THING FOR THE RAMUS INTERMEDIUS. IFR WAS 1.34, ALSO INDICATING NONSIGNIFICANT STENOSIS.; LEFT HEART CATHETERIZATION: THE LEFT MAIN: THE PATIENT HAS ACTUALLY NO LEFT MAIN. THE CIRCUMFLEX ARTERY, THE RAMUS INTERMEDIUS, AND THE LAD COME FROM SEPRATE OSTIA. ALL ARISE FROM THE LEFT CORONARY CUSP.; LEFT VENTRICULOGRAM: LEFT VENTRICULAR PRESSURE SYSTOLIC WAS 166, DIASTOLIC 9, END DIASTOLIC 17. AORTIC PRESSURE IS 158 OVER DIASTOLIC OF 49 WITH MEAN OF 92. NO GRADIENT ACROSS THE AORTIC VALVE. THERE WAS FAINT OPACIFICATION OF THE LEFT VENTRICLE. WE COULD NOT COMMENT ON THE LEFT VENTRICULAR FUNCTION.; SELECTIVE CORONARY ANGIOGRAPHY: THE OSTIUM OF THE LEFT ANTERIOR DESCENDING ARTERY APPEARED TO BE SUSPICIOUS. HOWEVER, THERE MAY BE 40% DISEASE IN SOME VIEWS. MILD AND DISTALLY, THERE IS NO SIGNIFICANT DISEASE. THE FIRST DIAGONAL HASNO SIGNIFICANT DISEASE.

| | |
|---|---|
| **AE Stopped Rx Day** | 114 (2 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 3 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | HISTORY OF MYOCARDIAL INFARCTION, ATRIAL FIBRILLATION AND CAROTID ARTERIAL DISEASE. |
| **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:** M15-572

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，胸痛の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，関節炎，糖尿病性ニューロパチー，高コレステロール血症，高血圧，甲状腺機能低下症，肥満，局面型乾癬，うつ病，乾癬性関節炎，糖尿病，心房細動，頚動脈疾患，心筋梗塞，元喫煙者（1 日 1 箱を 5 年間），非飲酒者，冠動脈疾患，ステント留置後状態及び高脂血症であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胸痛は消失した。

**退院時サマリーより：**20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸痛が 1 日続いたため救急治療室を受診した。被験者はニトログリセリンを投与されたが軽減は見られなかった。12 誘導心電図検査で RVR を伴う心房細動が認められ，心拍数は 118 回/分であった。被験者は ED にてカルディゼムを投与された。ED にて，血圧が 96/55，心拍数が 170 回/分，呼吸数が 16 回/分，体温が 97°F，パルスオキシメトリが 98%であった。心エコー検査では，駆出率が 55%～60%で，中等度の同心円状左室肥大が認められた。臨床検査の結果，CBC 及び BMP は正常で，ヘモグロビン A1C が 8.5，トロポニンが 0.027，再検査時のトロポニンが 0.169，0.245 であった。胸部 X 線検査で大動脈アテローム硬化症が認められたが，急性心肺疾患は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，心臓専門医による診察を受けた。胸痛は，ニトログリセリン投与下である程度軽減したものの持続した。20[redacted] 年 [redacted] 月 [redacted] 日，左心カテーテル検査が行われた。この検査で，RCA に留置されたステントの開存，鈍角枝の完全閉塞（側枝の状態は良好），左下行前動脈口及び中間枝口の著明ではない狭窄が認められた。被験者は，エリキュース及びプラビックスを継続し，アスピリンを中止するよう指示された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，restoril，ノルバスク，アミオダロン，ニトログリセリン，アミオダロン，prolonix 及びプラビックスであった。

Causality for UPADACITINIB (Blinded)

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1) Chest pain (10008479) (Chest pain (10008479) ) [v.22.1] [10008479]

**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)

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Event of CHEST PAIN

**- Investigator:** History of myocardial infarction, atrial fibrillation and carotid artery disease.

**- AbbVie:** Risk factors include pre-existing history of myocardial infarction, diabetes mellitus, hypertension, and hypercholesterolemia.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ALBUMIN:** 30 No units

[redacted] **20[redacted] ALK PHOS:** 135 No units

[redacted] **20[redacted] ALKALINE PHOSPHASTASE:** 135 No units

[redacted] **20[redacted] ALT:** 27 No units

**Unknown date BLOOD PRESSURE:** 96/55 bpm

**Unknown date BODY TEMPERATURE:** 97.0 F

[redacted] **20[redacted] BUN:** 23 No units

[redacted] **20[redacted] CALCIUM:** 8.8 No units

[redacted] **20[redacted] CARBON DIOXIDE:** 27 No units

**Unknown date CBC:** Normal

[redacted] **20[redacted] CHEST X-RAY:** NO ACUTE PULMONARY DISEASE. BORDERLINE CARDIOMEGALY.

[redacted] **20[redacted] CHLORIDE:** 106 No units

[redacted] **20[redacted] CREATININE:** 0.86 No units

[redacted] **20[redacted] ECHOCARDIOGRAM:** NORMAL LEFT VENTRICULAR SYSTOLIC FUNCTION. MODERATE ANNULAR CALCIFICATION. MILD THICKENING OF BOTH LEAFLET OF MITRAL VALVE WITH MILDLY REDUCED MOBILITY. MILDLY INCREASED LEFT ATRIAL SIZE. MODERATE CONCENTRIC LEFT VENTRICULAR HYPERTROPHY. AORTIC SCLEROSIS WITHOUT HEMODYNAMICALLY SIGNIFICANT STENOSIS AND NO SIGNIFICANT INSUFFICIENCY.

**Unknown date ECHOCARDIOGRAM:** Ejection fraction of 55% to 60%, moderate concentric left ventricular hypertrophy.

[redacted] 20[redacted] **EKG:** Atrial fibrillation with RVR with a rate of 118 beats per minute.

[redacted] 20[redacted] **ELECTROCARDIOGRAM:** A FIB WITH RAPID VENTRICULAR RESPONSE, LEFT AXIS DEVIATION, LBBB.

[redacted] 20[redacted] **ELECTROCARDIOGRAM:** NORMAL SINUS RHYTHM, LEFT AXIS DEVIATION, LEFT VENTRICULAR HYPERTROPHY WITH QRS WIDENING AND REPOLARIZATION ABNORMALITY.

[redacted] 20[redacted] **GLUCOSE:** 294 No units

[redacted] 20[redacted] **GLUCOSE:** 297 No units (normal 70 to 110)

[redacted] 20[redacted] **GLUCOSE:** 282 no units (normal 70 to 110)

[redacted] 20[redacted] **GLUCOSE:** 240 No units (normal 70 to 110)

**Unknown date HEART RATE:** 170 per min

**Unknown date HEMOGLOBIN A1C:** 8.5 No units

[redacted] 20[redacted] **INSTANTANEOUS FRACTIONAL FLOW RESERVE OF THE OSTIUM OF THE LEFT ANTERIOR DESCENDING ARTERY:** THE RIGHT CORONARY ARTERY IS A LARGE SIZE VESSEL, DOMINANT. IN THE PROXIMAL SEGMENT, THE STENTS ARE PATENT. DISTALLY, THERE IS NO SIGNIFICANT DISEASE. IT BIFUCRATES INTO A POSTERIOR DESCENDING ARTERY AND POSTEROLATERAL VESSEL WITH NO SIGNIFICANT DISEASE.

[redacted] 20[redacted] **INSTANTANEOUS FRACTIONAL FLOW RESERVE OF THE RAMUS INTERMEDIUS:** NORMALIZED THE WIRE BEFORE INSERTING THE GUIDE. ENGAGED THE OSTIUM OF THE LEFT ANTERIOR DESCENDING ARTERY. IFR WAS 0.95, INDICATING NONSIGNIFICANT STENOSIS. DID THE SAME THING FOR THE RAMUS INTERMEDIUS. IFR WAS 1.34, ALSO INDICATING NONSIGNIFICANT STENOSIS.

[redacted] 20[redacted] **LEFT VENTRICULOGRAM:** LEFT VENTRICULAR PRESSURE SYSTOLIC WAS 166, DIASTOLIC 9, END DIASTOLIC 17. AORTIC PRESSURE IS 158 OVER DIASTOLIC OF 49 WITH MEAN OF 92. NO GRADIENT ACROSS THE AORTIC VALVE. THERE WAS FAINT OPACIFICATION OF THE LEFT VENTRICLE. WE COULD NOT COMMENT ON THE LEFT VENTRICULAR FUNCTION.

[redacted] 20[redacted] **NEUT #:** 7.6 No units (normal 1.8 to 6.3)

[redacted] 20[redacted] **NEUTROPHILS:** 7.6 No units

[redacted] 20[redacted] **POTASSIUM:** 3.8 No units

[redacted] 20[redacted] **RBC:** 5.03 No units

[redacted] 20[redacted] **SELECTIVE CORONARY ANGIOGRAPHY:** THE OSTIUM OF THE LEFT ANTERIOR DESCENDING ARTERY APPEARED TO BE SUSPICIOUS. HOWEVER, THERE MAY BE 40% DISEASE IN SOME VIEWS. MILD AND DISTALLY, THERE IS NO SIGNIFICANT DISEASE. THE FIRST DIAGONAL HAS NO SIGNIFICANT DISEASE.

[redacted] 20[redacted] **SERUM TOTAL PROTEIN:** 6.4 No units

[redacted] **20[redacted] SODIUM:** 142 No units

[redacted] **20[redacted] TOTAL BILIRUBIN:** 0.5 No units

[redacted] **20[redacted] TROPONIN:** 0.169 NG/ML (normal 0 to 0.045)

[redacted] **20[redacted] TROPONIN:** 0.245 NG/ML (normal 0 to 0.045)

[redacted] **20[redacted] TROPONIN:** 0.234 NG/ML (normal 0 to 0.045)

**Unknown date TROPONINS:** 0.027 NG/ML (normal 0 to 0.045)

[redacted] **20[redacted] WBC:** 9.7 No units

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 |
|---|---|---|---|---|
| 意識変容状態 | X | | | |
| 大腸炎 | X | | | |
| 失神 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 15 mg QD | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| GASTROESOPHAGEAL REFLUX DISEASE | 20[redacted] |
| OTHER: INSOMNIA | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| OTHER: COLITIS | 20[redacted] |
| DEPRESSION: UNKNOWN | 20[redacted] |
| OTHER: CHRONIC BILATERAL SHOULDER PAIN | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: HYSTERECTOMY | 19[redacted] |
| SURGERY: RIGHT HIP REPLACEMENT | 20[redacted] |
| SURGERY: RIGHT KNEE REPLACEMENT | 20[redacted] |
| SURGERY: LEFT KNEE REPLACEMENT | 20[redacted] |
| SURGERY: OSTEOPENIA | 20[redacted] |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 173 | 173 |

| | | | | | |
|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 174 | [redacted]20[redacted] / 220 393 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 394 | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ESOMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted] |
| LORAZEPAM | 1 mg | QD | Y-M: 20[redacted] |
| ERGOCALCIFEROL | 2000 OTHER: UNITS | QD | Y-M: 20[redacted] |
| LISINOPRIL | 20 mg | QD | Y-M: 20[redacted] |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] |
| IBUPROFEN | 600 mg | QD | Y-M: 20[redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -204 |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] / -204 |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted] / -204 |

**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 |
|---|---|---|---|---|
| ESOMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| LORAZEPAM | 1 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| ERGOCALCIFEROL | 2000 OTHER: UNITS | QD | Y-M: 20[redacted] | NOT REPORTED |
| LISINOPRIL | 20 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| IBUPROFEN | 600 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -204 | NOT REPORTED |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] / -204 | NOT REPORTED |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted] / -204 | NOT REPORTED |
| AZTREONAM | 1 g | QD | Y-M: 20[redacted] / 234 | Y-M: 20[redacted] / 234 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / 234 | Y-M: 20[redacted] / 237 |
| MORPHINE | 2 mg | PRN | Y-M: 20[redacted] / 234 | Y-M: 20[redacted] / 237 |
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted] / 234 | Y-M: 20[redacted] / 237 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 234 | Y-M: 20[redacted] / 237 |
| CIPROFLOXACIN | 400 mg | QD | Y-M: 20[redacted] / 235 | Y-M: 20[redacted] / 235 |
| VICODIN | 1 OTHER: PILL | PRN | Y-M: 20[redacted] / 235 | Y-M: 20[redacted] / 237 |
| LOPERAMIDE | 4 mg | QD | Y-M: 20[redacted] / 236 | Y-M: 20[redacted] / 236 |
| DIPHENHYDRAMINE | 25 mg | PRN | Y-M: 20[redacted] / 236 | Y-M: 20[redacted] / 237 |
| LACTOBACILLUS ACIDOPHILUS | 2 OTHER: PILLS | QD | Y-M: 20[redacted] / 237 | NOT REPORTED |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] / 237 | Y-M: 20[redacted] / 244 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / 237 | Y-M: 20[redacted] / 247 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING OF MEDICAL CONDITION (COLITIS) |
| **Preferred term** | 大腸炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 231 |

| | |
|---|---|
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 234): Alanine Aminotransferase: 15 [0 - 40] U/L; Aspartate Aminotransferase: 18 [0 - 37] U/L; Blood Urea Nitrogen: 16.8 [2.9 - 7.1] MMOL/L; Creatinine: 186 [44 - 106] UMOL/L; Leukocytes: 15.1 [4.8 - 10.8] TH/CMM; Sodium: 128 [135 - 145] MMOL/L

**Microbiology**

[redacted]20[redacted] (RX DAY 234): BLOOD NPTST109-BLOOD CULTURE OF LEFT ARM: Negative; BLOOD NPTST110-BLOOD CULTURE OF RIGHT ARM: Negative

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 234): CT SCAN ABDOMEN/PELVIS: 1.DIFFUSE THICKENING OF THE WALL THE COLON WHICH WAS NONSPECIFIC HOWEVER MAY REPRESENT COLITIS. 2. HIATAL HERNIA

| | |
|---|---|
| **AE Stopped Rx Day** | 237 |
| **Duration of AE** | 7 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | WORSENING OF MEDICAL CONDITION (COLITIS) |
| **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** | SYNCOPE, ALTERED LEVEL OF CONSCIOUSNESS |
| **Preferred term** | 意識変容状態 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 359 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted](RX DAY 359): Blood Urea Nitrogen: 10 [2.5 - 6.4] MMOL/L; Hematocrit: 0.36 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 118 [120 - 160] G/L

**Microbiology**

[redacted]20[redacted](RX DAY 358): BLOOD NPTST105-BLOOD CULTURE: Negative; URINE NPTST670-URINE CULTURE: Negative

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 358): CHEST X RAY: CARDIOMEGALY WITH MILD PULMONARY VASCULAR CONGESTION. RADIOPAQUE RING STRUCTURE LIKELY OVERLIES THE PATIENT'S UPPER MEDIASTINUM.CORRELATION WITH DIRECT INSPECTION ON EXAM IS ADVISED.; CT SCAN HEAD: THERE IS MILD DIFFUSE CEREBRAL AND CEREBELLAR ATROPHY. THERE IS MILD SUBCORTICAL AND PERIVENTRICULAR WHITE MATTER HYPODENSITIES WITHIN THE BILATERALCEREBRAL HEMISPHERES WHICH IS NONSPECIFIC BUT LIKELYRELATED TO CHRONIC MICROVASCULAR DISEASE.

| | |
|---|---|
| **AE Stopped Rx Day** | 360 |
| **Duration of AE** | 2 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | SITE RECEIVED MEDICAL RECORDS.MEDICAL RECORDS REPORT THAT SUDDEN ONSET OF BRIEF LOSS OF CONSCIOUSNESS IN PATIENT ARE OF UNCLEAR ETIOLOGY. |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

**Event #3: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | SYNCOPE, ALTERED LEVEL OF CONSCIOUSNESS |
| **Preferred term** | 失神 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 359 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 359): Blood Urea Nitrogen: 10 [2.5 - 6.4] MMOL/L; Hematocrit: 0.36 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 118 [120 - 160] G/L

**Microbiology**

[redacted]20[redacted] (RX DAY 358): BLOOD NPTST105-BLOOD CULTURE: Negative; URINE NPTST670-URINE CULTURE: Negative

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 358): CHEST X RAY: CARDIOMEGALY WITH MILD PULMONARY VASCULAR CONGESTION. RADIOPAQUE RING STRUCTURE LIKELY OVERLIES THE PATIENT'S UPPER MEDIASTINUM.CORRELATION WITH DIRECT INSPECTION ON EXAM IS ADVISED.; CT SCAN HEAD: THERE IS MILD DIFFUSE CEREBRAL AND CEREBELLAR ATROPHY. THERE IS MILD SUBCORTICAL AND PERIVENTRICULAR WHITE MATTER HYPODENSITIES WITHIN THE BILATERALCEREBRAL HEMISPHERES WHICH IS NONSPECIFIC BUT LIKELYRELATED TO CHRONIC MICROVASCULAR DISEASE.

| | |
|---|---|
| **AE Stopped Rx Day** | 360 |
| **Duration of AE** | 2 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | SITE RECEIVED MEDICAL RECORDS.MEDICAL RECORDS REPORT THAT SUDDEN ONSET OF BRIEF LOSS OF CONSCIOUSNESS IN PATIENT ARE OF UNCLEAR 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:** M15-572

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，医学的状態の悪化（大腸炎）の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，胃食道逆流性疾患，大腸炎，高血圧，うつ病，局面型乾癬，乾癬性関節炎，非飲酒者及び非喫煙者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は医学的状態の悪化（大腸炎）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，医学的状態の悪化（大腸炎）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，3 日間に及ぶ重度の鋭い非放射状の左下腹部痛（疼痛スケール 7/10）のため入院した。被験者は悪心，嘔吐，悪寒及び血性下痢も発現していた。被験者によれば，発熱は見られなかった。被験者は，これは過去の大腸炎発作に似ていると述べた。抗生物質及び鎮痛薬の静脈内投与並びに水分補給が行われた。被験者は経口抗生物質に切り替えられた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，アズトレオナム，protonix，zofran，imodium，norco，モルヒネ，フラジール，CIPRO 及び lactobacillus であった。

Causality for UPADACITINIB (Blinded)

---

1) Colitis aggravated (10009890) (Colitis (10009887) ) [v.23.0] [10009890]

**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 WORSENING OF MEDICAL CONDITION (COLITIS)

**- Investigator:** WORSENING OF MEDICAL CONDITION (COLITIS)

**- AbbVie:** Event is more likely related to pre-existing history of colitis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] 20[redacted] **ALANINE AMINOTRANSFERASE:** 15 U/L (normal 0 to 40)

[redacted] 20[redacted] **ASPARTATE AMINOTRANSFERASE:** 18 U/L (normal 0 to 37)

[redacted] 20[redacted] **BLOOD CULTURE:** negative

[redacted] 20[redacted] **BUN:** 47 mg/dL (normal 8 to 20)

[redacted] 20[redacted] **CREATININE:** 2.1 mg/dL (normal 0.5 to 1.2)

[redacted] 20[redacted] **CT SCAN ABDOMEN/PELVIS:** 1.Diffuse thickening of the wall the colon which was nonspecific however may represent colitis. 2. Hiatal hernia

[redacted] 20[redacted] **SODIUM:** 128 MMOL/L (normal 135 to 145)

[redacted] 20[redacted] **WBC:** 15.1 TH/CMM (normal 4.8 to 10.8)
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，失神，意識レベルの変化の事象を発現した。

**Event 2 及び 3 の臨床経過：**

関連する病歴は，不眠症，高血圧，うつ病，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年[redacted] 月[redacted] 日であった。

20[redacted] 年[redacted] 月[redacted] 日，被験者は失神，意識レベルの変化を発現した。20[redacted] 年[redacted] 月[redacted] 日，失神，意識レベルの変化は消失した。

被験者はソファの上で身をかがめた状態で息子に発見された。反応がなく，2～3 分ほど覚醒しなかった。息子が 911 番通報し，被験者は救急診療科に搬送された。被験者は血圧が低かった。被験者は観察及び精密検査のため 20[redacted] 年[redacted] 月[redacted] 日に入院した。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。

被験者は線維筋痛に対し新たに薬剤（おそらくジアゼパム）を投与されており，本事象の原因がこの新しい薬剤にあるかもしれないと被験者は考えた。

Causality for UPADACITINIB (Blinded)

---

1) Syncope (10042772) (Syncope (10042772) ) [v.23.0] [10042772]

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

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

**Dechallenge:** Not Applicable

2) Altered state of consciousness (10001854) (Altered state of consciousness (10001854) ) [v.23.0] [10001854]

**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 SYNCOPE, ALTERED LEVEL OF CONSCIOUSNESS

**- Investigator:** SITE RECEIVED MEDICAL RECORDS.MEDICAL RECORDS REPORT THAT SUDDEN ONSET OF BRIEF LOSS OF CONSCIOUSNESS IN PATIENT ARE OF UNCLEAR ETIOLOGY.

**- AbbVie:** Risk factors include new prescription of sedating medication (diazepam noted by PI in source documents), pre-existing psoriasis, advanced age and hypertension.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **BLOOD CULTURE:** Negative

[redacted] **BLOOD PRESSURE:** 66/45 mmHg

[redacted] **BLOOD UREA NITROGEN:** 28 mg/dL (normal 7 to 18)

**[redacted] 20[redacted] CHEST X RAY:** Cardiomegaly with mild pulmonary vascular congestion. Radiopaque ring structure likely overlies the patients upper mediastinum. Correlation with direct inspection on exam was advised.

**[redacted] 20[redacted] CT SCAN HEAD:** Mild diffuse cerebral and cerebellar atrophy. Mild subcortical and periventricular white matter hypodensities within the bilateral cerebral hemispheres which was nonspecific but likely related to chronic microvascular disease.

**[redacted] 20[redacted] HEMATOCRIT:** 35.8 % (normal 37.0 to 47.0)

**[redacted] 20[redacted] HEMOGLOBIN:** 11.8 G/DL (normal 12.0 to 16.0)

**[redacted] 20[redacted] URINE CULTURE:** 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 |
|---|---|---|---|---|
| ブドウ球菌感染 | X | | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| ADA 40 mg EOW | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| HEPATITIS: HEPATITIS C | 19[redacted] |
| OTHER: CHRONIC　NECK PAIN | 20[redacted] |
| OTHER: CHRONIC BACK PAIN | 20[redacted] |
| OTHER: POST MENOPAUSAL | 20[redacted] |
| HYPOTHYROIDISM | 20[redacted] |
| KIDNEY DISORDER: CHRONIC KIDNEY DISEASE | 20[redacted] |
| OBESITY | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| Not reported. | |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | CURRENT | 0.2 PACK | 5[redacted] | |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 70 | 70 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| LEVOTHYROXINE | 300 ug | QD | Y-M: 20[redacted] |
| IBUPROFEN | 800 mg | TID | Y-M: 20[redacted] / -251 |

| | | | |
|---|---|---|---|
| APREMILAST | 30 mg | QD | Y-M: 20[redacted] / -134 |

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

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| LEVOTHYROXINE | 300 ug | QD | Y-M: 20[redacted] | ONGOING |
| IBUPROFEN | 800 mg | TID | Y-M: 20[redacted] / -251 | ONGOING |
| APREMILAST | 30 mg | QD | Y-M: 20[redacted] / -134 | ONGOING |

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

| | |
|---|---|
| **Event Description** | POSSIBLE STAPH INFECTION |
| **Preferred term** | ブドウ球菌感染 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 33 (17 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **SAE Supplemental Procedure** | |
| NOT REPORTED | |
| **AE Stopped Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | Unknown |
| **Relation to Study Drug by Investigator** | Unknown |
| **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:** M15-572

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，ブドウ球菌感染の可能性の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，C 型肝炎，甲状腺機能低下症，慢性腎臓病，肥満，局面型乾癬，乾癬性関節炎，現紙巻タバコ喫煙者（1 日 0.2 箱を 50 年間）及び禁酒であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はブドウ球菌感染の可能性を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，この被験者の治験薬の投与は完全に中止された。本報告時点でその他の詳細は提供されなかった。

Causality for ABT-494 (Blinded)

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1) Staphylococcal infection (10058080) (Staphylococcal infection (10058080) ) [v.21.1] [10058080]

**Causality as per reporter (Drug/Vaccine):** Not Reported

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

**Dechallenge:** No

Alternative Etiology for ABT-494 (Blinded)

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Event of POSSIBLE STAPH INFECTION

**- Investigator:** Not reported

**- AbbVie:** Risk factors include obesity, chronic kidney disease and current tobacco use.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] [redacted] **20[redacted] BODY WEIGHT:** 56.1 KG

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 |
|---|---|---|---|---|
| 虫垂炎 | X | | | X |

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

| Medical History | Onset Year |
|---|---|
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: HYPERLIPIDEMIA | 20[redacted] |
| OTHER: GALLSTONES | 20[redacted] |
| OTHER: DRUG RELATED HAIR LOSS | 20[redacted] |
| OTHER: TROCHANTERIC BURSITIS LEFT HIP | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: CHOLECYSTECTOMY | 20[redacted] |

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

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

**Study Drug Administration**

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

**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] |
| HYDROXYCHLOROQUINE | 200 mg | BID | Y-M: 20[redacted] |
| MELOXICAM | 15 mg | QD | Y-M: 20[redacted] |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] |
| METHOTREXATE | 17.5 mg | EVERY WEEK | Y-M: 20[redacted] |
| FOLINIC ACID | 5 mg | EVERY WEEK | Y-M: 20[redacted] / -336 |

**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] | NOT REPORTED |
| MELOXICAM | 15 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 113 |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] | ONGOING |
| METHOTREXATE | 17.5 mg | EVERY WEEK | Y-M: 20[redacted] | ONGOING |
| FOLINIC ACID | 5 mg | EVERY WEEK | Y-M: 20[redacted] / -336 | ONGOING |
| PIP/TAZO | UNKNOWN OTHER: UNKNOWN | OTHER: ONE TIME | Y-M: 20[redacted] / 21 | Y-M: 20[redacted] / 21 |
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted] / 22 | ONGOING |
| PARACETAMOL | 325 mg | PRN | Y-M: 20[redacted] / 22 | ONGOING |

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

**Event Description** ACUTE APPENDICITIS

**Preferred term** 虫垂炎

**AE Onset Date / Rx Day** [redacted]20[redacted] / 21

**Age at AE Onset** 5[redacted]

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 21): CT ABDOMEN/PELVIS WITH IV CONTRAST: MM DILATED APPENDIX WITH SURROUNDING INFLAMMATORY CHANGES SUSPICIOUS FOR ACUTE APPENDICITIS; [redacted]20[redacted] (RX DAY 22): LAPAROSCOPIC APPENDECTOMY: APPENDIX REMOVED

**AE Stopped Rx Day** 22

**Duration of AE** 2 DAYS

**Severity** Mild

**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]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，急性虫垂炎の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，乾癬性関節炎，高脂血症，非喫煙者及び飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性虫垂炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性虫垂炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右下腹部に放射状に拡がる臍周囲痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腹痛のため入院した。CT スキャンで虫垂炎が明らかとなり，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に腹腔鏡下虫垂切除術を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，ゾシン，zofran 及びタイレノールであった。

Causality for UPADACITINIB (Blinded)

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1) Acute appendicitis (10000677) (Appendicitis (10003011) ) [v.22.0] [10000677]

**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)

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Event of ACUTE APPENDICITIS

**- Investigator:** Not applicable

**- AbbVie:** Event is common in the general population.Relevant Laboratory & Other Diagnostic Tests

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**[redacted] 20[redacted] CT ABDOMEN/PELVIS WITH IV CONTRAST:** MM DILATED APPENDIX WITH SURROUNDING INFLAMMATORY CHANGES SUSPICIOUS FOR ACUTE APPENDICITIS

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 |
|---|---|---|---|---|
| 複視 | X | | | |

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

| Medical History | Onset Year |
|---|---|
| OTHER: FRACTURE RIGHT ANKLE | 19[redacted] |
| OTHER: FATTY TUMOR ON RING FINGER RIGHT HAND | 19[redacted] |
| MIGRAINE HEADACHE: OCCIPITAL AREA | 20[redacted] |
| MYOCARDIAL INFARCTION | 20[redacted] |
| OTHER: CARPAL TUNNEL LEFT WRIST | 20[redacted] |
| CORONARY ARTERY DISEASE: STABLE | 20[redacted] |
| DIABETES MELLITUS: TYPE II | 20[redacted] |
| HYPERLIPIDEMIA: STABLE | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| OTHER: COLON POLYPS | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| INCREASED CREATINE PHOSPHOKINASE: FRACTIONATED LAB TEST | NOT REPORTED |
| SURGERY: FRACTURE RIGHT ANKLE REPAIR | 19[redacted] |
| SURGERY: FATTY TUMOR ON RING FINGER RIGHT HAND REMOVED | 19[redacted] |
| SURGERY: CARPAL TUNNEL LEFT WRIST SURGERY | 20[redacted] |
| SURGERY: COLON POLYPS REMOVED | 20[redacted] |
| SURGERY: CARPAL TUNNEL SURGERY LEFT WRIST | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 20 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 169 | 169 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 170 | [redacted]20[redacted] / 397 | 228 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 398 | | |

**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] |
| CLOPIDOGREL | 75 mg | QD | Y-M: 20[redacted] |
| METOPROLOL | 25 mg | BID | Y-M: 20[redacted] |
| HEPATITIS B IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| METFORMIN | 1000 mg | QD | Y-M: 20[redacted] |
| METFORMIN | 1500 mg | QD | Y-M: 20[redacted] |
| CALCIPOTRIOL | 0.005 % | QD | Y-M: 20[redacted] |
| CLOBETASOL | 0.05 % | BID | Y-M: 20[redacted] |
| LOTRISONE | 1/0.05 % | BID | Y-M: 20[redacted] / -359 |
| APREMILAST | 30 mg | BID | Y-M: 20[redacted] / -206 |
| EZETIMIBE | 10 mg | QD | Y-M: 20[redacted] / -116 |
| ROSUVASTATIN | 40 mg | QD | Y-M: 20[redacted] / -116 |

**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 |
| METOPROLOL | 25 mg | BID | Y-M: 20[redacted] | NOT REPORTED |
| CLOPIDOGREL | 75 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 167 |
| METFORMIN | 1000 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| METFORMIN | 1500 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| EZETIMIBE | 10 mg | QD | Y-M: 20[redacted] / -116 | NOT REPORTED |
| ROSUVASTATIN | 40 mg | QD | Y-M: 20[redacted] / -116 | NOT REPORTED |
| DAPAGLIFLOZIN | 5 mg | QD | Y-M: 20[redacted] / 144 | NOT REPORTED |
| CLOPIDOGREL | 75 mg | QD | Y-M: 20[redacted] / 174 | NOT REPORTED |
| ACETYLSALICYLIC ACID | 325 mg | QD | Y-M: 20[redacted] / 174 | Y-M: 20[redacted] / 174 |
| GADOBUTROL | 9 mmol | QD | Y-M: 20[redacted] / 175 | Y-M: 20[redacted] / 175 |
| INSULIN | 3 OTHER: UNITS | PRN | Y-M: 20[redacted] / 175 | Y-M: 20[redacted] / 177 |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | DIPLOPIA |
| **Preferred term** | 複視 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 172 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 174): CT HEAD: PROPTOSIS BILATERALLY OF UNCERTAIN CLINICAL SIGNIFICANCE, SMALL FAT-CONTAINING FOCUS IN THE CEREBELLAR CISTERN MEASURING APPROXIMATELY 7 MM WITHOUT MASS EFFECT OR EDEMA WHICH IS COMPLETELY FAT DENSITY;[redacted]20[redacted] (RX DAY 175): ANGIO HEAD WITH CONTRAST MRI: UNREMARKABLE MR ANGIOGRAM HEAD; CAROTID ULTRASOUND: ATHEROSCLEROTIC IRREGULARITY THE RIGHT AND LEFT INTERAL CAROTID ARTERY WITHOUT EVIDENCE FOR LUMINAL STENOSIS; OCCUPATIONAL THERAPY EVALUATION: COMPLETED; PHYSICAL THERAPY EVALUATION: COMPLETED

| | |
|---|---|
| **AE Stopped Rx Day** | 177 |
| **Duration of AE** | 6 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | CORONARY ARTERY DISEASE |
| **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:** M15-572

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，複視の事象を発現した。

**Event 2 の臨床経過：**

関連する病歴は，元喫煙者（1 日 1 箱を 20 年間），冠動脈疾患，心筋梗塞，2 型糖尿病，高脂血症，高血圧，局面型乾癬，乾癬性関節炎，現飲酒者（1 日 2 杯未満）及び心臓発作（兄弟が 50 歳の時）の家族歴であった。心筋梗塞の家族歴もあった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は複視を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，複視は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は悪心，嘔吐，後頭部痛，複視及び回転性めまいを発現した。治験責任医師によると，被験者は，視線が右側に偏っており，複数回の嘔吐と，歩行時の右方向への傾きも見られたと報告した。治験責任医師によると，被験者の妻は，被験者には右側顔面

下垂が見られたが，喚語困難は見られなかったと報告した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，複数の画像検査が行われた。また，理学療法及び作業療法による評価も行われた。また治験責任医師からは，被験者は本事象発現時にプラビックスを服用していなかったと報告された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，アスピリン，クロピドグレル及びインスリンであった。

Causality for UPADACITINIB (Blinded)

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1) Diplopia (10013036) (Diplopia (10013036) ) [v.22.1] [10013036]

**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 DIPLOPIA

**- Investigator:** CORONARY ARTERY DISEASE

**- AbbVie:** risk factors include pre-existing hypertension and diabetes mellitus.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ANGIO HEAD WITHOUT CONTRAST MRI:** UNREMARKABLE MR ANGIOGRAM HEAD

[redacted] **20[redacted] CAROTID ULTRASOUND:** ATHEROSCLEROTIC IRREGULARITY THE RIGHT AND LEFT INTERAL CAROTID ARTERY WITHOUT EVIDENCE FOR LUMINAL STENOSIS

[redacted] **20[redacted] CT HEAD:** PROPTOSIS BILATERALLY OF UNCERTAIN CLINICAL SIGNIFICANCE, SMALL FAT-CONTAINING FOCUS IN THE CEREBELLAR CISTERN MEASURING APPROXIMATELY 7 MM WITHOUT MASS EFFECT OR EDEMA WHICH IS COMPLETELY FAT DENSITY

[redacted] **20**[redacted] **ECG:** Abnormal. T wave abnormality. Short QT interval

**Unknown date ECHOCARDIOGRAM:** Results not reported

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 |
|---|---|---|---|---|
| 腰部脊柱管狭窄症 | X | X | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 15 mg QD | 4[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: CHICKEN POX | 19[redacted] |
| OTHER: LEFT SPASTIC HEMIPARESIS | 19 |
| OTHER: TRAMATIC BRAIN INJURY | 19 |
| DEPRESSION: STABLE | 20 |
| OTHER: PLAQUE PSORASIS | 20 |
| CHOLELITHIASIS: CHOLECYSTITIS | 20 |
| OTHER: APPENDICITIS | 20 |
| OTHER: IRON DEFICIENCY ANEMIA | 20 |
| OTHER: BILATERAL CARPAL SYNDROME | 20 |
| DEGENERATIVE DISC DISEASE: LUMBAR SPINE | 20 |
| OTHER: LUMBOSACRAL SPINAL STENOSIS | 20 |
| PSORIATIC ARTHRITIS | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: LEFT VALGUS MALALIGNMENT | 20[redacted] |
| SURGERY: TIBIAL OSTEOTOMY | 20 |
| SURGERY: APPENDECTOMY | 20 |
| SURGERY: BILATERAL TUBAL LIGATION | 20 |
| SURGERY: CHOLECYSTECTOMY | 20 |
| SURGERY: BILATERAL CARPAL SYNDROME SURGERY | 20 |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | CURRENT | 0.05 PACK | 29 | |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 1 | [redacted] / 172 | 172 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 173 | [redacted] / 395 | 223 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 396 | [redacted] / 563 | 168 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| BUPROPION | 150 mg | QD | Y-M: 20[redacted] |
| SERTRALINE | 100 mg | QD | Y-M: 20[redacted] |
| BACLOFEN | 10 mg | TID | Y-M: 20[redacted] |
| TIZANIDINE | 8 mg | QD | Y-M: 20[redacted] |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] |
| TRAMADOL | 50 mg | QD | Y-M: 20[redacted] |
| GABAPENTIN | 300 mg | TID | Y-M: 20[redacted] |
| IBUPROFEN | 400 mg | QD | Y-M: 20[redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -116 |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] / -116 |

**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 |
|---|---|---|---|---|
| BUPROPION | 150 mg | QD | Y-M: 20[redacted] | ONGOING |
| SERTRALINE | 100 mg | QD | Y-M: 20[redacted] | ONGOING |
| BACLOFEN | 10 mg | TID | Y-M: 20[redacted] | ONGOING |
| TIZANIDINE | 8 mg | QD | Y-M: 20[redacted] | ONGOING |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] | ONGOING |
| TRAMADOL | 50 mg | QD | Y-M: 20[redacted] | ONGOING |
| GABAPENTIN | 300 mg | TID | Y-M: 20[redacted] | ONGOING |
| IBUPROFEN | 400 mg | QD | Y-M: 20[redacted] | ONGOING |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -116 | ONGOING |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] / -116 | ONGOING |
| DOCUSATE | 100 mg | BID | Y-M: 20[redacted] / 565 | ONGOING |
| PARACETAMOL | 975 mg | QID | Y-M: 20[redacted] / 565 | ONGOING |
| CEFAZOLIN | 2 g | QD | Y-M: 20[redacted] / 565 | Y-M: 20[redacted] / 567 |
| MORPHINE | 2 mg | QD | Y-M: 20[redacted] / 565 | Y-M: 20[redacted] / 567 |
| ONDANSETRON | 4 mg | QD | Y-M: 20[redacted] / 565 | Y-M: 20[redacted] / 567 |
| SODIUM CHLORIDE | 0.9 % | QD | Y-M: 20[redacted] / 565 | Y-M: 20[redacted] / 567 |
| OXYCODONE | 5 mg | TID | Y-M: 20[redacted] / 567 | ONGOING |
| SENNA ALEXANDRINA | 17.2 mg | OTHER: QHS | Y-M: 20[redacted] / 567 | ONGOING |

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

| | |
|---|---|
| **Event Description** | WORSENING OF LUMBOSACRAL SPINAL STENOSIS |

| | |
|---|---|
| **Preferred term** | 腰部脊柱管狭窄症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 531 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 567): Calcium: 2.25 [2.17 - 2.67] MMOL/L; Creatinine: 38 [44 - 106] UMOL/L; Glucose: 8.4 [3.9 - 5.5] MMOL/L; Hematocrit: 0.38 [0.31 - 0.46] FRACTION OF 1; Hemoglobin: 129 [117 - 155] G/L; Leukocytes: 10.6 [4.3 - 10.8] 10^9/L; NPTST146-CARBON DIOXIDE: 28 [24 - 32] MMOL/L; NPTST242-EGFR: 90 [89 - 90] (ML/MIN/BSA); NPTST430-MCV (MEAN CORPUSCULAR VOLUME): 91.4 [80 - 100] FL; Platelets: 168 [140 - 440] 10^9/L; Potassium: 3.5 [3.5 - 5.3] MMOL/L; Sodium: 140 [135 - 145] MMOL/L

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 564): X-RAY LUMBOSACRAL SPINE: WORSENING OF LUMBOSACRAL SPINAL STENOSIS STENOSIS; [redacted]20[redacted] (RX DAY 565): BILATERAL L4/S1 LAMINECTOMIES: SUCCESSFUL; RIGHT SIDED L5/S1 DISCECTOMY: SUCCESSFUL

| | |
|---|---|
| **AE Stopped Rx Day** | 568 (5 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 38 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | LUMBAR-RADICULOPATHY DUE TO H/O OF LUMBAR SACRAL SPINAL STENOSIS |
| **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:** M15-572

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，腰仙部脊柱管狭窄症の悪化の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，左痙性不全片麻痺，外傷性脳損傷，局面型乾癬，鉄欠乏性貧血，腰椎椎間板変性疾患，腰仙部脊柱管狭窄症，現喫煙者（1 日 0.05 箱 29 年間）及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腰仙部脊柱管狭窄症の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，腰仙部脊柱管狭窄症の悪化は消失した。

本治験への組入れ前において，被験者には 20[redacted] 年 [redacted] 月より腰仙部脊柱管狭窄症の病歴があった。

腰仙部脊柱管狭窄症が悪化し，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に入院した。徴候・症状は右下肢錯感覚及び背部痛であった。同日，被験者は両側 L4～L5 の椎弓切除術及び右側 L5～S1 の椎間板切除術を受けた。手術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。本事象により治験薬の投与は完全に中止された。

治験責任医師によると，この被験者における本事象の危険因子は背部痛であった。

投与された薬剤はオキシコドン，塩化ナトリウム，モルヒネ及びセファゾリンであった。

Causality for UPADACITINIB (Blinded)

---

1) Lumbosacral spinal stenosis (10081628) (Lumbar spinal stenosis (10025005) ) [v.22.1] [10081628]

**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 OF LUMBOSACRAL SPINAL STENOSIS

**- Investigator:** Lumbar radiculopathy due to history of lumbar sacral spinal stenosis

**- AbbVie:** event is more likely related to pre-existing lumbosacral spinal stenosis. Pre-existing psoriatic arthritis is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] CREATININE:** 0.43 mg/dL (normal 0.50 to 1.20)

[redacted] **20[redacted] GLUCOSE:** 152 mg/dL (normal 70 to 99)

[redacted] **20[redacted] X-RAY LUMBOSACRAL SPINE:** WORSENING OF LUMBOSACRAL SPINAL STENOSIS STENOSIS

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 |
|---|---|---|---|---|
| 形質細胞性骨髄腫 | X | X | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 30 mg QD | 7[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: CHICKEN POX | 19[redacted] |
| OTHER: PLAQUE PSORIASIS | 19[redacted] |
| MIGRAINE HEADACHE | 19[redacted] |
| OTHER: ANXIETY | 20[redacted] |
| OTHER: POSTMENOPAUSAL | 20[redacted] |
| GASTROESOPHAGEAL REFLUX DISEASE | 20[redacted] |
| OTHER: RIGHT CARPAL TUNNEL SYNDROME | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| HYPERLIPIDEMIA: STABLE | 20[redacted] |
| OTHER: LEFT CARPAL TUNNEL SYNDROME | 20[redacted] |
| DEGENERATIVE DISC DISEASE: LUMBAR SPINE | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| OTHER: IRON DEFICIENCY ANEMIA | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: RIGHT CARPAL TUNNEL REPAIR | 20[redacted] |
| SURGERY: LEFT CARPAL TUNNEL REPAIR | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 22 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 168 | 168 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 169 | [redacted]20[redacted] / 393 | 225 |

| | | | | | |
|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 394 | [redacted]20[redacted] / 712 | 319 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| METHOTREXATE | 15 mg | QD | Y-M: 19[redacted] |
| AXOTAL | 1 OTHER: TABLET | PRN | Y-M: 19[redacted] |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] |
| CALCIUM | 600 mg | BID | Y-M: 20[redacted] |
| LORAZEPAM | 0.5 mg | QD | Y-M: 20[redacted] |
| MAGNESIUM | 500 mg | QD | Y-M: 20[redacted] |
| RANITIDINE | 150 mg | QD | Y-M: 20[redacted] |
| BIOTIN | 500 mEq | QD | Y-M: 20[redacted] |
| ERGOCALCIFEROL | 2000 IU | QD | Y-M: 20[redacted] |
| VERAPAMIL | 120 mg | QD | Y-M: 20[redacted] |
| ESOMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted] |
| ASCORBIC ACID | 500 mg | QD | Y-M: 20[redacted] |
| IBUPROFEN | 400 mg | QD | Y-M: 20[redacted] |
| IRON | 325 mg | QD | Y-M: 20[redacted] |
| EZETIMIBE | 10 mg | QD | Y-M: 20[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 |
|---|---|---|---|---|
| AXOTAL | 1 OTHER: TABLET | PRN | Y-M: 19[redacted] | ONGOING |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] | ONGOING |
| CALCIUM | 600 mg | BID | Y-M: 20[redacted] | ONGOING |
| LORAZEPAM | 0.5 mg | QD | Y-M: 20[redacted] | ONGOING |
| MAGNESIUM | 500 mg | QD | Y-M: 20[redacted] | ONGOING |
| BIOTIN | 500 mEq | QD | Y-M: 20[redacted] | ONGOING |
| ERGOCALCIFEROL | 2000 IU | QD | Y-M: 20[redacted] | ONGOING |
| VERAPAMIL | 120 mg | QD | Y-M: 20[redacted] | ONGOING |
| ESOMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted] | ONGOING |
| ASCORBIC ACID | 500 mg | QD | Y-M: 20[redacted] | ONGOING |
| IBUPROFEN | 400 mg | QD | Y-M: 20[redacted] | ONGOING |
| IRON | 325 mg | QD | Y-M: 20[redacted] | ONGOING |
| EZETIMIBE | 10 mg | QD | Y-M: 20[redacted] / -62 | ONGOING |
| DENOSUMAB | 60 mg | OTHER: Q 6 MONTHS | Y-M: 20[redacted] / 65 | ONGOING |
| SERTRALINE | 50 mg | QD | Y-M: 20[redacted] / 425 | ONGOING |
| FAMOTIDINE | 40 mg | QD | Y-M: 20[redacted] / 644 | ONGOING |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Possible Malignancy, Event of Interest - Malignancy, Event of Interest - Malignancy excluding NMSC**

| | |
|---|---|
| **Event Description** | MULTIPLE MYELOMA |
| **Preferred term** | 形質細胞性骨髄腫 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 677 |

| | |
|---|---|
| **Age at AE Onset** | 7[redacted] |

**Laboratory Testing**
NOT REPORTED
**Microbiology**
NOT REPORTED
**SAE Supplemental Procedure**
[redacted]20[redacted] (RX DAY 677): BONE MARROW BIOPSY: MYLOMA INDICATED; [redacted]20[redacted] (RX DAY 714): PETSCAN: MYLOMA OBSERVED

| | |
|---|---|
| **AE Stopped Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | OTHER MEDICALLY IMPORTANT SERIOUS EVENT |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，多発性骨髄腫の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，局面型乾癬，元喫煙者（1 日 1 箱を 22 年間），乾癬性関節炎，高血圧及び飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は多発性骨髄腫を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は骨髄生検を受け，多発性骨髄腫が判明した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は白血球数減少及び多発性骨髄腫のため入院した。同日，被験者は退院した。本報告の時点で，被験者は多発性骨髄腫の治療を受けていなかった。治験薬の投与が完全に中止された。

**The patient's past medications include:**

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 19[redacted] - [redacted] 19[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Multiple myeloma (10028228) (Plasma cell myeloma (10035226) ) [v.23.0] [10028228]

**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 MULTIPLE MYELOMA

**- Investigator:** Not applicable

**- AbbVie:** In the medical literature the etiologic factors for multiple myeloma are not well established. Subject's advanced age is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BONE MARROW BIOPSY:** Myeloma indicated

[redacted] **20[redacted] HEMOGLOBIN:** 10.7 G/DL (normal 11.5 to 15.8)

[redacted] **20[redacted] HEMOGLOBIN:** 10.7 G/DL (normal 11.5 to 15.8)

[redacted] **20[redacted] LYMPHOCYTES:** 0.45 x10x3/ul (normal 0.80 to 3.00)

[redacted] **20[redacted] LYMPHOCYTES:** 0.71 x10x3/ul (normal 0.80 to 3.00)

[redacted] **20[redacted] LYMPHOCYTES:** 0.64 x10x3/ul (normal 0.80 to 3.00)

[redacted] **20[redacted] LYMPHOCYTES:** 0.38 x10x3/ul (normal 0.80 to 3.00)

[redacted] **20[redacted] NEUTROPHILS:** 1.36 x10x3/ul (normal 1.96 to 7.23)

[redacted] **20[redacted] NEUTROPHILS:** 1.55 x10x3/ul (normal 1.96 to 7.23)

[redacted] **20[redacted] PET SCAN:** Myloma observed.

[redacted] **20[redacted] WBC:** 1.89 x10x3/ul (normal3.80 to 10.70)

[redacted] **20[redacted] WBC:** 2.03 x10x3/ul (normal 3.80 to 10.70)

[redacted] **20[redacted] WBC:** 3.33 x10x3/ul (normal 3.80 to 10.70)

[redacted] **20[redacted] WBC:** 3.68 x10x3/ul (normal 3.80 to 10.70)

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 |
|---|---|---|---|
| UPA 15 mg QD | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: RESTLESS LEG SYNDROME | 19[redacted] |
| OTHER: CHICKEN POX | 19 |
| OTHER: CLAVICLE FRACTURE | 19 |
| OTHER: EXCESSIVE FATIGUE | 20 |
| OTHER: INSOMNIA | 20 |
| DIABETES MELLITUS | 20 |
| OTHER: PLAQUE PSORIASIS | 20 |
| HYPOTHYROIDISM | 20 |
| OTHER: CARPAL TUNNEL | 20 |
| HYPERTENSION | 20 |
| OTHER: DEGENERATIVE JOINT DISEASE | 20 |
| PSORIATIC ARTHRITIS | 20 |
| OTHER: RIGHT PINKY FRACTURE | 20 |
| OTHER: LEFT SHOULDER PAIN | 20 |
| OTHER: LEFT SHOULDER STEROID SHOT | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: LEFT ELBOW ARTHROSCOPY | 20[redacted] |
| SURGERY: LEFT KNEE ARTHROSCOPY | 20 |
| SURGERY: CARPEL TUNNEL SURGERY ON LEFT HAND | 20 |
| SURGERY: CHOLECYSTECTOMY | 20 |
| SURGERY: GALL BLADDER SURGERY | 20 |

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

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 168 | 168 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 169 | [redacted]20[redacted] / 399 | 231 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 400 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PRAMIPEXOLE | 1 mg | BID | Y-M: 19[redacted] |
| CYANOCOBALAMIN | 1 OTHER: TABLET | QD | Y-M: 19[redacted] |
| MINERALS NOS W/VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 19[redacted] |
| HEPATITIS B IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| INDOMETACIN | 75 mg | PRN | Y-M: 20[redacted] |
| LEVOTHYROXINE | 100 OTHER: MCG | PRN | Y-M: 20[redacted] |
| TRAMADOL | 50 mg | QD | Y-M: 20[redacted] |
| HYDROCHLOROTHIAZIDE | 25 mg | PRN | Y-M: 20[redacted] |
| METFORMIN | 500 mg | PRN | Y-M: 20[redacted] |
| LOSARTAN | 25 mg | PRN | Y-M: 20[redacted] |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -322 |
| FOLIC ACID | 800 OTHER: MCG | QD | Y-M: 20[redacted] / -105 |

**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 |
|---|---|---|---|---|
| PRAMIPEXOLE | 1 mg | BID | Y-M: 19[redacted] | NOT REPORTED |
| CYANOCOBALAMIN | 1 OTHER: TABLET | QD | Y-M: 19[redacted] | NOT REPORTED |
| MINERALS NOS W/VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 19[redacted] | NOT REPORTED |
| INDOMETACIN | 75 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| LEVOTHYROXINE | 100 OTHER: MCG | PRN | Y-M: 20[redacted] | NOT REPORTED |
| TRAMADOL | 50 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| HYDROCHLOROTHIAZIDE | 25 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| METFORMIN | 500 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| LOSARTAN | 25 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -322 | Y-M: 20[redacted] / 917 |

| | | | | |
|---|---|---|---|---|
| FOLIC ACID | 800 OTHER: MCG | QD | Y-M: 20[redacted] / - 105 | NOT REPORTED |
| PIPERACILLIN W/TAZOBACTAM | 3.375 G / 15 ML OTHER: G/ML | QD | Y-M: 20[redacted] / 79 | Y-M: 20[redacted] / 81 |
| LEVOFLOXACIN | 750 MG / 150 ML OTHER: MG/ML | QD | Y-M: 20[redacted] / 80 | Y-M: 20[redacted] / 80 |
| VANCOMYCIN | 1500 MG / 250 ML OTHER: MG/ML | QD | Y-M: 20[redacted] / 81 | Y-M: 20[redacted] / 81 |

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

| | |
|---|---|
| **Event Description** | PNEUMONIA |
| **Preferred term** | 肺炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 77 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

[redacted]20[redacted] (RX DAY 77): BLOOD NPTST105-BLOOD CULTURE: Negative-NO GROWTH AT 5 DAYS;
20[redacted] (RX DAY 79): URINE NPTST670-URINE CULTURE: Negative-NO GROWTH <1000 ORGANISMS/ML

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 78): CHEST X RAY: INTERVAL INCREASE IN SIZE OF RIGHT MIDDLE LOBE PNEUMONIA; CT CHEST WITH CONTRAST: RIGHT MIDDLE LOBE PNEUMONIA; [redacted]20[redacted] (RX DAY 80): CHEST X-RAY: STABLE RIGHT MIDDLE LOBE PNEUMONIA

| | |
|---|---|
| **AE Stopped Rx Day** | 81 |
| **Duration of AE** | 5 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，肺炎の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，糖尿病，局面型乾癬，甲状腺機能低下症，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。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

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。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 5 日間に及ぶ症状の悪化による発熱及び全身の脱力に伴う非湿性咳嗽で救急治療室を受診した。同日，被験者は退院した。咳嗽及び発熱の悪化は持続した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はさらなる管理のため ER を受診することにした。胸部 CT スキャン検査が行われ，右肺中葉肺炎の徴候が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。治療が行われ，被験者の状態は改善した。20[redacted] 年 [redacted] 月 2 日，被験者は退院した。

投与された薬剤は，バンコマイシン，levaquin 及びゾシンであった。

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:** rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

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Event of PNEUMONIA

**- Investigator:** Not applicable

**- AbbVie:** Risk factors include age and diabetes mellitus (Marrie, TJ. epidemiology, pathogenesis and microbiology of community acquired pneumonia in adults in uptodate, post TW (ED), uptodate, Waltham, MA)

Relevant Laboratory & Other Diagnostic Tests

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**Unknown date BLOOD CULTURE:** Negative

[redacted] **20[redacted] CHEST X RAY:** Interval increase in size of right middle lobe pneumonia.

[redacted] **20[redacted] CHEST X-RAY:** Stable right middle lobe pneumonia.

[redacted] **20[redacted] CT CHEST WITH CONTRAST:** Right Middle Lobe Pneumonia

**Unknown date URINE CULTURE:** 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 |
|---|---|---|---|---|
| 乳房蜂巣炎 | X | X | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 15 mg QD | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: CHICKEN POX | 19[redacted] |
| OTHER: MUMPS | 19 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO AMINOGLYCOSIDE | 19 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO PENICILLIN | 19 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO SULFA DRUGS | 19 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO BIAXIN | 19 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO DOXYCICLINE | 19 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO KEFLEX | 19 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO LEVAQUIN | 19 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO MAXROBID | 19 |
| OTHER: ALLERGIC RHINITIS | 19 |
| OTHER: FATTY LIVER | 19 |
| OTHER: CHOLELITHIASIS | 19 |
| HYPERTENSION | 19 |
| OTHER: HYPERLIPIDEMIA | 20 |
| OTHER: DEPRESSION | 20 |
| OTHER: CHRONIC GENERALIZED PAIN | 20 |
| OTHER: ACID REFLUX | 20 |
| PSORIATIC ARTHRITIS | 20 |
| OTHER: NAUSEA | 20 |
| OTHER: SUPERFICIAL AND DEEP PERIVASCULAR AND PERIFOLLICULAR LYMPHOCYTIC DERMATITIS | 20 |
| OTHER: ATYPICAL NEVUS | 20 |
| OTHER: BENIGN NEOPLASM OF SKIN | 20 |
| OTHER: COMPOUND NEVUS WITH ATYPICAL MELANOCYTIC HYPERPLASIA | 20 |
| OTHER: FIBROUS PAPULE | 20 |
| OTHER: OPEN COMEDONE | 20 |
| OTHER: SKIN TAG | 20 |
| OTHER: DERMAL HYPERSENSITIVITY REACTION | 20 |
| OTHER: PALMOPLANTAR PUSTULOSIS | 20 |
| OTHER: ANAL FISSURE | 20 |
| OTHER: DERMATITIS | 20 |
| OTHER: MYOCARDIAL BRIDGE | 20 |
| OTHER: IRRITATED SEBORRHOIC KERATITIS | 20 |

| | |
|---|---|
| OTHER: BOIL | 20[redacted] |
| OTHER: ABNORMAL LIVER FUNCTION TEST | 20[redacted] |
| OTHER: ANXIETY | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| OTHER: PSORIATIC SPONDYLITIS | 20[redacted] |
| OTHER: GENITAL HERPES | 20[redacted] |
| OTHER: LICHEN SCLEROSUS | 20[redacted] |
| OTHER: ACUTE BRONCHITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: CHOLECYSTECTOMY | 19[redacted] |
| SURGERY: HYSTERECTOMY | 19[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | CURRENT | 1 PACK | 48.5 | |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 77 | 77 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ESOMEPRAZOLE | 40 mg | QD | Y-M: 20[redacted] |
| METOPROLOL | 25 mg | QD | Y-M: 20[redacted] |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] |
| AMLODIPINE | 5 mg | QD | Y-M: 20[redacted] |
| ERGOCALCIFEROL | 400 OTHER: UNITS/ML | QD | Y-M: 20[redacted] |
| PANADEINE CO | 300/30 mg | PRN | Y-M: 20[redacted] |
| PREGABALIN | 75 mg | QD | Y-M: 20[redacted] |
| PROMETHAZINE | 25 mg | PRN | Y-M: 20[redacted] |
| SERTRALINE | 50 mg | QD | Y-M: 20[redacted] |
| CLOBETASOL | 0.05 % | PRN | Y-M: 20[redacted] |
| APREMILAST | 30 mg | QD | Y-M: 20[redacted] |
| HERPES ZOSTER IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MUPIROCIN | 2 % | PRN | Y-M: 20[redacted] |
| VALACICLOVIR | 500 mg | QD | Y-M: 20[redacted] / -80 |

| | | | |
|---|---|---|---|
| LOCAL ANESTHETICS | 0.3 % | PRN | Y-M: 20[redacted] / -28 |
| DOXYCYCLINE | 100 mg | BID | Y-M: 20[redacted] / -16 |

**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 |
|---|---|---|---|---|
| ESOMEPRAZOLE | 40 mg | QD | Y-M: 20[redacted] | ONGOING |
| METOPROLOL | 25 mg | QD | Y-M: 20[redacted] | ONGOING |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] | ONGOING |
| AMLODIPINE | 5 mg | QD | Y-M: 20[redacted] | ONGOING |
| ERGOCALCIFEROL | 400 OTHER: UNITS/ML | QD | Y-M: 20[redacted] | ONGOING |
| PANADEINE CO | 300/30 mg | PRN | Y-M: 20[redacted] | ONGOING |
| PREGABALIN | 75 mg | QD | Y-M: 20[redacted] | ONGOING |
| PROMETHAZINE | 25 mg | PRN | Y-M: 20[redacted] | ONGOING |
| SERTRALINE | 50 mg | QD | Y-M: 20[redacted] | ONGOING |
| APREMILAST | 30 mg | QD | Y-M: 20[redacted] | ONGOING |
| MUPIROCIN | 2 % | PRN | Y-M: 20[redacted] | ONGOING |
| VALACICLOVIR | 500 mg | QD | Y-M: 20[redacted] / -80 | ONGOING |
| LOCAL ANESTHETICS | 0.3 % | PRN | Y-M: 20[redacted] / -28 | ONGOING |
| DOCUSATE | 100 mg | PRN | Y-M: 20[redacted] / 34 | Y-M: 20[redacted] / 87 |
| DOXYCYCLINE | 100 mg | BID | Y-M: 20[redacted] / 73 | Y-M: 20[redacted] / 77 |
| LEVETIRACETAM | 500 mg | QD | Y-M: 20[redacted] / 73 | Y-M: 20[redacted] / 77 |
| VANCOMYCIN | 750 mg/kg | OTHER: Q12H | Y-M: 20[redacted] / 78 | Y-M: 20[redacted] / 82 |
| MORPHINE | 2 mg | OTHER: Q4H PRN | Y-M: 20[redacted] / 78 | Y-M: 20[redacted] / 88 |
| ATORVASTATIN | 10 mg | QD | Y-M: 20[redacted] / 78 | Y-M: 20[redacted] / 91 |
| PREGABALIN | 75 mg | BID | Y-M: 20[redacted] / 79 | ONGOING |
| DIPHENHYDRAMINE | 25 mg | BID | Y-M: 20[redacted] / 79 | Y-M: 20[redacted] / 79 |
| ZOLPIDEM | 5 mg | PRN | Y-M: 20[redacted] / 79 | Y-M: 20[redacted] / 83 |
| CLONIDINE | 0.1 mg | OTHER: Q4H PRN | Y-M: 20[redacted] / 91 | ONGOING |
| PITAVASTATIN | 2 mg | QD | Y-M: 20[redacted] / 91 | ONGOING |
| DAPTOMYCIN | 450 mg | QD | Y-M: 20[redacted] / 92 | Y-M: 20[redacted] / 99 |

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

| | |
|---|---|
| **Event Description** | LEFT BREAST CELLULITIS |
| **Preferred term** | 乳房蜂巣炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 73 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 47): Hematocrit: 0.43 [0.36 - 0.46] FRACTION OF 1; [redacted]20[redacted] (RX DAY 78): Basophils/Leukocytes: 0.6 [0.2 - 1] %; Creatinine: 85 [53 - 115] UMOL/L; Eosinophils/Leukocytes: 1.5 [0.9 - 2.9] %; Erythrocytes: 5.1 [4.2 - 5.4] 10^12/L; Hemoglobin: 132 [120 - 160] G/L; Ketones: NEGATIVE [NOT REPORTED - NOT REPORTED] NEGATIVE; Leukocytes: 6.7 [3 - 12] 10^9/L; Lymphocytes/Leukocytes: 35.5 [20.5 - 45.5] %; Monocytes/Leukocytes: 5.3 [5.5 - 11.7] %; Neutrophils/Leukocytes: 56.8 [43 - 65] %; Platelets: 274 [130 - 400] 10^9/L; Specific Gravity: 1.020 [1 - 1.03] UNIT NOT REPORTED

**Microbiology**

[redacted]20[redacted] (RX DAY 78): WOUND NPTST698-WOUND CULTURE: Positive-WOUND CULTURE SHOWS THAT PATIENT HAS ABSCESS GRAM STAIN: 1. RARE WBC'S/RARE GRAM POSITIVE COCCI/ NO EPITHELIAL CELLS 2. CORYNEBACTERIUM SPECIES RARE/DIPHTHEROIDS NO FURTHER WORKUP;[redacted]20[redacted] (RX DAY 83): WOUND NPTST699-WOUND CULTURE (GRAM STAIN FINAL: Positive-RARE WBC'S RARE GRAM POSITIVE COCCI, NO EPITHELIAL CELLS; [redacted]20[redacted] (RX DAY 86): WOUND NPTST215-CULTURE WOUND FINAL: Positive-CORYNEBACTERIUM SPECIES RARE/DIPHTHEROIDS NO FURTHER WORKUP; [redacted]20[redacted] (RX DAY 90): BLOOD NPTST105-BLOOD CULTURE: Negative-NO GROWTH AFTER 5 DAYS

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 78): CHEST X-RAY, 1 VIEW: MINIMAL SCARRING OR ATELECTASIS IN THE LINGULA BUT OTHERWISE NORMAL CHEST, THE CARDIOVASCULAR SILHOUETTE IS NORMAL.; CXR 2 VIEWS: HISTORY PROVIDED: LEFT BREAST CELLULITIS FINDINGS: THERE IS NO INFILTRATE OR ATELECTASIS. THE HEART SIZE IS NORMAL. THERE IS NO VASCULAR CONGESTION. THERE IS NO PLEURAL EFFUSION. CONCLUSION: NORMALEXAM; [redacted]20[redacted] (RX DAY 80): ULTRA SOUND BREAST W AX LTD UNI LT: INDICATION: MASTOIDITIS VERSUS ABSCESS LEFT BREAST FINDINGS: 4.4 X 1.8 X 0.5 CM HYPOECHOIC AREA WITHIN THE DERMIS COMPATIBLE WITH PHLEGMONOUS CELLULITIS. NO AXILLARY ADENOPATHY. IMPRESSIONS: INFLAMMATORY LESION OF THE SKIN. ASSESSMENT: ACR BI-RADS CATEOGRY 2 - BENIGN; [redacted]20[redacted] (RX DAY 82): INCISION AND DRAINAGE OF LEFT BREAST ABSCESS: REMOVED THE BREAST TISSUE AND WOUND CULTURES

| | |
|---|---|
| **AE Stopped Rx Day** | 112 (35 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 40 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，左乳房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，乾癬性関節炎，表在型・深部型の血管周囲性・毛包周囲性リンパ球性皮膚炎，皮膚過敏症反応，皮膚炎，刺激反応性の脂漏性角化症，局面型乾癬，硬化性苔癬，現喫煙者（1 日 1 箱を 48.5 年間）及び元飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された

皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左乳房蜂巣炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左乳房蜂巣炎は消失した。

入院前に，左乳房乳頭周囲の下側に水疱が出現し悪化した。被験者はかかりつけ医を受診した。ドキシサイクリンの投与が開始されたが，被験者はこの薬剤に忍容性が認められなかった。水疱は改善せず，乳房が赤くなって炎症を起こした。被験者は専門医を受診し，炎症を伴う左乳房水疱，倦怠感，発汗，体の疼き及び痛みなどの症状のため 20[redacted] 年 [redacted] 月 [redacted] 日に入院した。感染症及び一般外科手術のための診察が開始された。また，抗生物質の静脈内投与及び温湿布による治療も開始されたが，膿瘍が出現した。20[redacted] 年 [redacted] 月 [redacted] 日，左乳房膿瘍の切開及びドレナージが行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，ジフェンヒドラミン，ゾルピデム酒石酸塩，プレガバリン，モルヒネ，ケプラ，ドキシサイクリン，バンコマイシン及びダプトマイシンであった。

**The patient's past medications include:**

DOXYCYCLINE for UNKNOWN INDICATION

MAXROBID for UNKNOWN INDICATION

LEVAQUIN for UNKNOWN INDICATION

KEFLEX for UNKNOWN INDICATION

BIAXIN for UNKNOWN INDICATION

AMINOGLYCOSIDE for UNKNOWN INDICATION

PENICILLIN for UNKNOWN INDICATION

SULFA for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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1) Cellulitis breast (10007903) (Breast cellulitis (10006217) ) [v.21.1] [10007903]

**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)

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Event of LEFT BREAST CELLULITIS

**- Investigator:** Not applicable

**-AbbVie:** Risk factors include obesity (BMI 37.9 at screening), advanced age and current smoker.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] BLOOD CULTURE:** Negative. No growth after 5 days.

[redacted] **20[redacted] CHEST X-RAY, 1 VIEW:** MINIMAL SCARRING OR ATELECTASIS IN THE LINGULA BUT OTHERWISE NORMAL CHEST, THE CARDIOVASCULAR SILHOUETTE IS NORMAL.

[redacted] **20[redacted] CXR 2 VIEWS:** HISTORY PROVIDED: LEFT BREAST CELLULITIS FINDINGS: THERE IS NO INFILTRATE OR ATELECTASIS. THE HEART SIZE IS NORMAL. THERE IS NO VASCULAR CONGESTION. THERE IS NO PLEURAL EFFUSION. CONCLUSION: NORMAL EXAM

[redacted] **20[redacted] ULTRASOUND BREAST WITH AX LTD UNI LT:** INDICATION: MASTOIDITIS VERSUS ABSCESS LEFT BREAST FINDINGS: 4.4 X 1.8 X 0.5 CM HYPOECHOIC AREA WITHIN THE DERMIS COMPATIBLE WITH PHLEGMONOUS CELLULITIS. NO AXILLARY ADENOPATHY. IMPRESSIONS: INFLAMMATORY LESION OF THE SKIN. ASSESSMENT: ACR BI-RADS CATEOGRY 2 - BENIGN

[redacted] **20[redacted] WOUND CULTURE:** Positive. wound culture shows that patient has abscess. 1. Rare WBC's/rare gram positive cocci/no epithelial cells. 2. Corynebacterium species rare/diphtheroids. No further workup.

[redacted] **20[redacted] WOUND CULTURE (GRAM STAIN FINAL):** positive. Rare WBC's. Rare gram positive cocci, no epithelial cells.

[redacted] **20[redacted] WOUND CULTURE FINAL:** Positive. Corynebacterium species rare/diphtheroids. No further workup.

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

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 帯状疱疹 | X | | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 15 mg QD | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: CHICKEN POX | 19[redacted] |
| EYE DISEASE/DISORDER: LAZY EYE (LEFT) | 19[redacted] |
| OTHER: POST-MENOPAUSAL | 20[redacted] |
| OTHER: DACTYLITIS - MIDDLE FINGER OF RIGHT HAND | 20[redacted] |
| OTHER: FLAT FEET - BILATERAL | 20[redacted] |
| OTHER: SKIN - PLAQUE PSORIASIS (ELBOWS - BILATERAL) | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: VITAMIN D DEFICIENCY | 20[redacted] |
| OBESITY: ABDOMEN - OVERWEIGHT - BENIGN | 20[redacted] |
| CARDIAC ARRHYTHMIA: AFIB - ACUTE ONSET APR 2017/RECENT ECGS SHOW NSR/ NOT RECURRENT SINCE APR 2017 - TAKING METOPROLOL AND CLEARED BY PT'S CARDIOLOGIST | 20[redacted] |
| OTHER: SUBLUXATION OF 1ST CARPOMETACARPAL JOINT IN LEFT HAND | 20[redacted] |
| OTHER: CALCIFIED AORTA | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: CATARACT - LEFT EYE | 20[redacted] |
| SURGERY: CATARACT - RIGHT EYE | 20[redacted] |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 168 | 168 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 169 | [redacted]20[redacted] / 392 | 224 |
| ABT-494 | 15 MG | 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 | 650 mg | PRN | Y-M: 19[redacted] |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] |
| ERGOCALCIFEROL | 2000 IU | OTHER: 6 DAYS PER WEEK | Y-M: 20[redacted] |
| ERGOCALCIFEROL | 50000 IU | EVERY WEEK | Y-M: 20[redacted] |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted] |
| LEFLUNOMIDE | 20 mg | OTHER: THREE TIMES PER WEEK | Y-M: 20[redacted] |
| HERPES ZOSTER IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] / -359 |
| FOLIC ACID | 800 ug | QD | Y-M: 20[redacted] / -301 |
| METHOTREXATE | 7.5 mg | EVERY WEEK | Y-M: 20[redacted] / -208 |
| METOPROLOL | 25 mg | BID | Y-M: 20[redacted] / -149 |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] / -90 |
| METHOTREXATE | 10 mg | EVERY WEEK | Y-M: 20[redacted] / -87 |

**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] | NOT REPORTED |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| ERGOCALCIFEROL | 2000 IU | OTHER: 6 DAYS PER WEEK | Y-M: 20[redacted] | NOT REPORTED |
| ERGOCALCIFEROL | 50000 IU | EVERY WEEK | Y-M: 20[redacted] | NOT REPORTED |
| FOLIC ACID | 800 ug | QD | Y-M: 20[redacted] / -301 | NOT REPORTED |
| METOPROLOL | 25 mg | BID | Y-M: 20[redacted] / -149 | NOT REPORTED |
| METHOTREXATE | 10 mg | EVERY WEEK | Y-M: 20[redacted] / -87 | NOT REPORTED |
| ATORVASTATIN | 10 mg | QD | Y-M: 20[redacted] / 638 | NOT REPORTED |
| ERYTHROMYCIN | 1/3 INCH OF OINTMENT OTHER: CM | OTHER: 6 TIMES PER DAY | Y-M: 20[redacted] / 942 | Y-M: 20[redacted] / 954 |
| ACICLOVIR | 1 g | OTHER: Q8H | Y-M: 20[redacted] / 942 | Y-M: 20[redacted] / 956 |

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

| | |
|---|---|
| **Event Description** | SHINGLES |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 939 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 945): Alanine Aminotransferase: 25 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Alkaline Phosphatase: 44 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Aspartate Aminotransferase: 45 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Bilirubin: 0.9 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Blood Urea Nitrogen: 8 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Calcium: 6.4 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Chloride: 102 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Creatinine: 0.4 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hematocrit: 30 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 10.8 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 3.3 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST176-CO2: 20 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST195-COVID SCREENING: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST402-LACTIC ACID: 1.5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST558-RAPID INFLUENZA A & B: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST664-URINALYSIS: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 109 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Potassium: 3.3 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Sodium: 133 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Rx Day** | 950 |
| **Duration of AE** | 12 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，帯状疱疹の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，水疱瘡，閉経後，乾癬性関節炎，ビタミン D 欠乏，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹は消失した。

入院前，被験者はかかりつけの眼科医を受診し左眼ヘルペスと診断されていた。診断は病歴と身体的診察に基づいてなされた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 102.7°F の発熱，倦怠感，すでに診断を受けていた左眼ヘルペスのため ER を受診した。同日，被験者は入院した。被験者はバルトレックスを投与されていたが症状は改善せず，被験者を救急治療室（ER）に連れてきた夫は，被験者の行動がおかしい（精神状態に変調を来している）と述べた。診察の結果，被験者は意識清明で，人・場所・時間の見当識障害はなかった。入院時，被験者は精神状態に全く変調を来していなかった。被験者は，眼ヘルペスによる自身の不快感について話すことができたが，苦しんでいる様子はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

経過観察のための来院時，被験者の前額部の病変は乾燥しており，左目尻にわずかに腫脹が見られた。眼ヘルペスの症状は顔面の皮膚にのみ見られた。

被験者には水疱瘡の既往歴があり，20[redacted] 年 [redacted] 月に帯状疱疹ワクチンを接種していた。

投与された薬剤は，エリスロマイシン及びアシクロビルであった。

**The patient's past medications include:**

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

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

Causality for UPADACITINIB (Blinded)

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1) Shingles (10040555) (Herpes zoster (10019974) ) [v.23.0] [10040555]

**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)

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Event of SHINGLES

**- Investigator:** Not Applicable

**- AbbVie:** Not applicable.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 44 no unit

[redacted] **20[redacted] ALT:** 25 no unit

[redacted] **20[redacted] AST:** 45 no unit

[redacted] **20[redacted] BILIRUBIN:** 0.9 no unit

[redacted] **20[redacted] BLOOD PRESSURE:** 140/72 mm/Hg

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 8 no unit

[redacted] **20[redacted] BODY TEMPERATURE:** 102.7 F

[redacted] **20[redacted] BODY TEMPERATURE:** 99.1 F

[redacted] **20[redacted] CALCIUM:** 6.4 no unit

[redacted] **20[redacted] CHLORIDE:** 102 no unit

[redacted] **20[redacted] CO2:** 20 no unit

[redacted] **20[redacted] COVID SCREENING:** Negative

[redacted] **20[redacted] CREATININE:** 0.4 no unit

[redacted] **20[redacted] HEART RATE:** 64 /min

[redacted] **20[redacted] HEMATOCRIT:** 30 no unit

[redacted] **20[redacted] HEMOGLOBIN:** 10.8 no unit

[redacted] **20[redacted] LACTIC ACID:** 1.5 no unit

[redacted] **20[redacted] O2 SATURATION:** 97 %

[redacted] **20[redacted] PLATELET COUNT:** 109 no unit

[redacted] **20[redacted] POTASSIUM:** 3.3 no unit

[redacted] **20[redacted] RAPID INFLUENZA:** Influenza A & B: Negative

[redacted] **20[redacted] RESPIRATORY RATE:** 16 /min

[redacted] **20[redacted] SODIUM:** 133 no unit

[redacted] **20[redacted] URINALYSIS:**Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3.3 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 |
|---|---|---|---|---|
| 背部痛 | X | | | |

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

| Medical History | Onset Year |
|---|---|
| SLEEP APNEA: OBSTRUCTIVE SLEEP APNEA | 19[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: TINGLING LEFT JAWBONE | 20[redacted] |
| OTHER: LEFT KNEE ARTHROCENTESIS | 20[redacted] |
| OTHER: LEFT KNEE ARTHROCENTESIS | 20[redacted] |
| OTHER: BLOOD BLISTERS INNER THIGHS BILATERAL | 20[redacted] |
| OTHER: ALLERGIC RHINITIS (INTERMITTENT) | 20[redacted] |
| OTHER: COLONOSCOPY (NORMAL) | 20[redacted] |
| OTHER: ERECTILE DYSFUNCTION | 20[redacted] |
| OTHER: SHORTNESS OF BREATH (RESTRICTIVE DUE TO OBESITY) | 20[redacted] |
| OTHER: STRESS ECHO TEST (NORMAL) | 20[redacted] |
| HYPERLIPIDEMIA | 20[redacted] |
| OTHER: DYSPNEA | 20[redacted] |
| OBESITY | 20[redacted] |
| OTHER: HYPERCHOLESTEREMIA | 20[redacted] |
| OTHER: RIGHT OLECRANON BURSA ASPIRATED | 20[redacted] |
| OTHER: INFLAMMATORY BURSITIS | 20[redacted] |
| OTHER: LEFT KNEE ARTHROCENTESIS | 20[redacted] |
| OSTEOARTHRITIS | 20[redacted] |
| OTHER: BACK PAIN | 20[redacted] |
| OTHER: FLEXION CONTRACTURE LEFT KNEE | 20[redacted] |
| OTHER: BLEPHARITIS OV- OCULAR ROSACEA RELATED | 20[redacted] |
| OTHER: OCULAR HYPERTENSION- BORDERLINE OV WITH PIGMENT DISPERSION | 20[redacted] |
| OTHER: PIGMENT DISPERSION SYNDROME BILATERAL | 20[redacted] |
| OTHER: ACNE ROSACEA | 20[redacted] |
| OTHER: CHRONIC NASAL CONGESTION | 20[redacted] |
| OTHER: NASAL SEPTAL DEVIATION | 20[redacted] |
| OTHER: SEASONAL ALLERGIC RHINITIS DUE TO POLLEN | 20[redacted] |
| OTHER: RIGHT KNEE ARTHROCENTESIS | 20[redacted] |
| OTHER: RIGHT KNEE PAIN | 20[redacted] |
| OTHER: LEFT KNEE ARTHROCENTESIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| Not reported. | |

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

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted] / 1 | [redacted] / 171 | 171 |
| ABT-494 | 30 MG | ORAL | QD | [redacted] / 172 | [redacted] / 385 | 214 |
| ABT-494 | 30 MG | ORAL | QD | [redacted] / 386 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MELOXICAM | 15 mg | QD | Y-M: [redacted] |
| METHOTREXATE | 12.5 mg | EVERY WEEK | Y-M: [redacted] |
| METHOTREXATE | 17.5 mg | EVERY WEEK | Y-M: [redacted] |
| METHOTREXATE | 17.5 mg | EVERY WEEK | Y-M: [redacted] |
| TARS | 1 % | EVERY WEEK | Y-M: [redacted] |
| DICLOFENAC | 75 mg | BID | Y-M: [redacted] |
| BETAMETHASONE | 1 OTHER: TSP | EVERY WEEK | Y-M: [redacted] |
| DIPHTHERIA VACCINE TOXOID W/PERTUSS | 0.5 mL | OTHER: ONE TIME ONLY | Y-M: [redacted] |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: [redacted] |
| INFLUENZA VACCINE | 0.5 OTHER: MC | OTHER: ONE TIME ONLY | Y-M: [redacted] |
| ATORVASTATIN | 40 mg | QD | Y-M: [redacted] |
| PNEUMOCOCCAL VACCINE | 0.5 mL | OTHER: ONE TIME ONLY | Y-M: [redacted] |
| AVANAFIL | 100 mg | PRN | Y-M: [redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: [redacted] |
| FLUTICASONE | 1 OTHER: SPRAYS | PRN | Y-M: [redacted] |
| LORATADINE | 10 mg | QD | Y-M: [redacted] |
| MINOCYCLINE | 50 mg | QD | Y-M: [redacted] |
| COLECALCIFEROL | 2000 OTHER: UNIT | QD | Y-M: [redacted] / -215 |
| FISH OIL | 1000 mg | QD | Y-M: [redacted] / -215 |
| VITAMINS NOS | 200 mg | QD | Y-M: [redacted] / -215 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: [redacted] / -161 |
| PREDNISONE | 5 mg | QD | Y-M: [redacted] / -161 |

| | | | |
|---|---|---|---|
| TRIAMCINOLONE | 80 mg | OTHER: ONE TIME ONLY | Y-M: 20[redacted] / -84 |

**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 |
|---|---|---|---|---|
| DICLOFENAC | 75 mg | BID | Y-M: 20[redacted] | NOT REPORTED |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 759 |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| LORATADINE | 10 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| COLECALCIFEROL | 2000 OTHER: UNIT | QD | Y-M: 20[redacted] / -215 | NOT REPORTED |
| FISH OIL | 1000 mg | QD | Y-M: 20[redacted] / -215 | NOT REPORTED |
| VITAMINS NOS | 200 mg | QD | Y-M: 20[redacted] / -215 | NOT REPORTED |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -161 | NOT REPORTED |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] / -161 | NOT REPORTED |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 224 | NOT REPORTED |
| ROSUVASTATIN | 20 mg | OTHER: QHS | Y-M: 20[redacted] / 398 | NOT REPORTED |
| MINOCYCLINE | 50 mg | QD | Y-M: 20[redacted] / 400 | NOT REPORTED |
| SILDENAFIL | 20 mg | PRN | Y-M: 20[redacted] / 497 | NOT REPORTED |
| CLINDAMYCIN | 1 % | PRN | Y-M: 20[redacted] / 522 | NOT REPORTED |
| LISINOPRIL | 10 mg | QD | Y-M: 20[redacted] / 595 | NOT REPORTED |
| METHYLPREDNISOLONE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] / 667 | Y-M: 20[redacted] / 667 |
| GUAIFENESIN | 600 mg | PRN | Y-M: 20[redacted] / 727 | Y-M: 20[redacted] / 737 |
| PROMETHAZINE W/CODEINE | 5 mg | PRN | Y-M: 20[redacted] / 733 | Y-M: 20[redacted] / 737 |
| AMOXICILLIN | 875 mg | BID | Y-M: 20[redacted] / 733 | Y-M: 20[redacted] / 739 |
| METHOCARBAMOL | 500 mg | QD | Y-M: 20[redacted] / 745 | Y-M: 20[redacted] / 752 |

**Event #1: Serious Adverse Event**

**Event Description** WORSENING LOW BACK PAIN

**Preferred term** 背部痛

**AE Onset Date / Rx Day** [redacted]20[redacted] / 689

**Age at AE Onset** 5[redacted]

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 758): MRI LUMBAR SPINE WITHOUT CONTRAST: MRI SHOWED MODERATE LUMBAR SPONDYLOSIS, MILD/MODERATE MULTILEVEL DEGENERATIVE CHANGES AND LARGE DISC EXTRUSION AT L4-5 RESULTS IN SEVERE SPINAL CANAL STENOSIS. ALSO SHOWED MODERATE/SEVERE NARROWING OFTHE THECAL SAC AT L2-3 AND L3-4 PREDOMINATELY FROM POSTERIOR EPIDURAL LIPOMATOSIS AND SHORT PEDICLES AND MILD TO SEVERE FORAMINAL STENOSIS.; [redacted]20[redacted] (RX DAY 759): L4-5 DECOMPRESSIVE LAMINECTOMY BILATERAL MICRO-DISCECTOMY: RESOLVED

**AE Stopped Rx Day** 761

**Duration of AE** 73 DAYS

**Severity** Mild

**Relation to Study Drug by Investigator** No Reasonable Possibility

**Investigator Alternative Etiology** LOW BACK PAIN

**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:** M15-572

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，腰痛の悪化の事象を発現した。

**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，肥満，背部痛，変形性関節症，左膝屈曲拘縮，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腰痛の悪化を発現した。

被験者には 20[redacted] 年 [redacted] 月から背部痛があった。20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日までの間に腰痛が悪化した。

20[redacted] 年 [redacted] 月 [redacted] 日，腰部から下肢にかけての疼痛が増強し，重度で筋力に影響を及ぼす進行性の脱力が出現した。被験者は腰痛悪化のため理学療法を受けた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は脱力及び下肢まで放散する疼痛のため救急治療室を受診した。歩行できず，ベッドから出ることもできなかった。被験者は入院した。腰椎 MRI が行われ，中等度の腰椎症，軽度／中等度の多段階退行性変化及び L4～5 椎間板突出による重度の脊柱管狭窄症が認められた。MRI では，L2～3 と L3～4 に中等度から重度の硬膜嚢狭小化も認められ，これは主に後方の硬膜外脂肪腫症と椎弓根の短縮によるものであった。また，軽度から重度の椎間孔狭窄が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は除圧的椎弓切除術・両側顕微鏡下椎間板切除術

を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，腰痛の悪化は消失した。

投与された薬剤は，メトカルバモールであった。

**The patient's past medications include:**

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

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

BETHAMASONE VALERATE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted]20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Back pain aggravated (10048412) (Back pain (10003988) ) [v.23.0] [10048412]

**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)

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Event of WORSENING LOW BACK PAIN

**- Investigator:** Low back pain

**- AbbVie:** Event more likely related to pre-existing back pain (diagnosed in 20[redacted]). Obesity is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] [redacted] **20[redacted]MRI LUMBAR SPINE WITHOUT CONTRAST:** MRI showed moderate lumbar spondylosis, mild/moderate multilevel degenerative changes and large disc extrusion at L4-5 results in severe spinal canal stenosis. Also showed moderate/severe narrowing of the thecal sac at L2-3 and L3-4 predominately from posterior epidural lipomatosis and short pedicles and mild to severe foraminal stenosis.

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 |
|---|---|---|---|---|
| 消化不良 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 15 mg QD | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| DRUG ALLERGIES/REACTIONS: ALLERGY TO PENECILLIN | 19[redacted] |
| HEPATITIS: NOT SURE WHICH | 19 |
| HYPERTENSION | 19 |
| OBESITY | 19 |
| OTHER: BENIGN TUMOR STATUS POST SURGERY. | 19 |
| SEIZURE DISORDER/CONVULSIONS: SEIZURES | 19 |
| OTHER: PLAQUE PSORIASIS | 19 |
| SLEEP APNEA | 19 |
| OTHER: POST MENOPAUSAL | 19 |
| GASTROESOPHAGEAL REFLUX DISEASE: GERD | 19 |
| OTHER: FOOT FRACTURE (RIGHT) | 20 |
| OTHER: IRRITABLE BOWEL SYNDROME | 20 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO CODEINE | 20 |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO DULOXETINE | 20 |
| OSTEOARTHRITIS: AFFECTING MULTIPLE JOINTS | 20 |
| OTHER: MERALGIA PARESTHETICA | 20 |
| PSORIATIC ARTHRITIS | 20 |
| DEPRESSION: CHRONIC | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: GALL BLADDER REMOVAL SURGERY | 19[redacted] |
| SURGERY: BRAIN SURGERY FOR BENIGN BRAIN TUMOR | 19 |
| SURGERY: SURGERY FOR REPAIR OF DETACHED RETINA RIGHT EYE. | 20[redacted] |

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

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 1 | [redacted] / 168 | 168 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 169 | [redacted] / 392 | 224 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 393 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| OMEPRAZOLE | 20 mg | QD | Y-M: 19[redacted] |
| HYOSCYAMINE | 0.375 mg | BID | Y-M: 20[redacted] |
| AZILSARTAN | 40 mg | QD | Y-M: 20[redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] |
| LEVETIRACETAM | 750 mg | QD | Y-M: 20[redacted] / -338 |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] / -247 |
| METHOTREXATE | 17.5 mg | EVERY WEEK | Y-M: 20[redacted] / -193 |

**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 |
|---|---|---|---|---|
| OMEPRAZOLE | 20 mg | QD | Y-M: 19[redacted] | NOT REPORTED |
| AZILSARTAN | 40 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 805 |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| LEVETIRACETAM | 750 mg | QD | Y-M: 20[redacted] / -338 | NOT REPORTED |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] / -247 | NOT REPORTED |
| METHOTREXATE | 17.5 mg | EVERY WEEK | Y-M: 20[redacted] / -193 | Y-M: 20[redacted] / 281 |
| DICYCLOVERINE | 10 mg | PRN | Y-M: 20[redacted] / 29 | NOT REPORTED |
| VALACICLOVIR | 800 mg | TID | Y-M: 20[redacted] / 281 | Y-M: 20[redacted] / 299 |
| METHOTREXATE | 17.5 mg | EVERY WEEK | Y-M: 20[redacted] / 299 | NOT REPORTED |

**Event #1: Serious Adverse Event**

**Event Description** GASTRIC INDIGESTION

**Preferred term** 消化不良

**AE Onset Date / Rx Day** [redacted] / 79

**Age at AE Onset** 6[redacted]

**Laboratory Testing**

[redacted] (RX DAY 79): Blood Urea Nitrogen: 9.3 [1.4 - 7.5] MMOL/L; Chloride: 109 [95 - 108] MMOL/L; Erythrocytes: 3.9 [4.2 - 5.4] 10^12/L; NPTST427-MCH: 33 [27 - 31] PG; NPTST454-MPV: 8.6 [9.4 - 12.4] FL; NPTST646-TROPONIN I: 0.05 [0 - 0.05] NG/ML

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted] (RX DAY 80): CARDIAC CATHETERIZATION: NEGATIVE FINDINGS.

**AE Stopped Rx Day** 80

| | |
|---|---|
| **Duration of AE** | 2 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | SUBJECT HAD EATEN HEAVY MEAL CONSISTING OF PIZZA AND THEREAFTER COMPLAINED OF LEFT LOWER CHEST PAIN. |
| **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:** M15-572

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，胃消化障害の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，高血圧，痙攣発作，睡眠時無呼吸，胃食道逆流性疾患，乾癬性関節炎及び非喫煙者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胃消化障害を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胃消化障害は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左側胸痛を訴えた。被験者は救急治療室を受診し，評価のため一晩入院した。心臓に原因は見当たらなかった。20[redacted] 年 [redacted] 月 [redacted] 日，心カテーテル検査が行われたが，異常所見は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for UPADACITINIB (Blinded)

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1) Indigestion (10021706) (Dyspepsia (10013946) ) [v.22.1] [10021706]

**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 GASTRIC INDIGESTION

**- Investigator:** SUBJECT HAD EATEN HEAVY MEAL CONSISTING OF PIZZA AND THEREAFTER COMPLAINED OF LEFT LOWER CHEST PAIN.

**- AbbVie:** event is more likely related to pre-existing gastro esophageal reflux disease.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] CARDIAC CATHETERIZATION:** Negative findings

[redacted] **20[redacted] MPV:** 8.6 FL (normal <12.4)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.85 10^6/mm3 (normal 4.20 to 5.40)

[redacted] **20[redacted] TROPONIN:** <0.050 ng/ml

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

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 細菌性肺炎 | X | | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 15 mg QD | 8[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: TONSILITIS | 19[redacted] |
| OTHER: APPENDICITIS | 19[redacted] |
| DRUG ALLERGIES/REACTIONS: PENECILLIN | 19[redacted] |
| DRUG ALLERGIES/REACTIONS: SULFA DRUGS | 19[redacted] |
| CONGESTIVE HEART FAILURE | 19[redacted] |
| OTHER: HYPERCHOLESTEROLEMIA | 19[redacted] |
| OTHER: CROHNS DISEASE | 20[redacted] |
| OTHER: DERMATITIS | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: VITAMIN D DEFFICIENCY | 20[redacted] |
| OSTEOARTHRITIS: BILATERAL HANDS | 20[redacted] |
| OSTEOPOROSIS | 20[redacted] |
| DEGENERATIVE DISC DISEASE | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: TONCILECTOMY | 19[redacted] |
| SURGERY: APPENDECTOMY | 19[redacted] |
| SURGERY: STENT PLACEMENTS | 19[redacted] |
| SURGERY: PARTIAL COLECTOMY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 2 PACK | 35 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 1 | [redacted] / 169 | 169 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 170 | [redacted] / 392 | 223 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 393 | | |

**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: 19[redacted] |
| METOPROLOL | 25 mg | QD | Y-M: 19[redacted] |
| PRAVASTATIN | 80 mg | QD | Y-M: 19[redacted] |
| MESALAZINE | 1000 mg | TID | Y-M: 20[redacted] |
| PARACETAMOL | 200 mg | PRN | Y-M: 20[redacted] |
| HYDROXYCHLOROQUINE | 200 mg | BID | Y-M: 20[redacted] |
| METHOTREXATE | 7.5 mg | OTHER: WEEKLY | Y-M: 20[redacted] |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] |
| ERGOCALCIFEROL | 2000 IU | QD | Y-M: 20[redacted] |
| PREDNISONE | 1 mg | QD | Y-M: 20[redacted] |
| TRAMADOL | 50 mg | BID | Y-M: 20[redacted] |
| IBANDRONIC ACID | 150 mg | OTHER: MONTHLY | 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: 19[redacted] | NOT REPORTED |
| METOPROLOL | 25 mg | QD | Y-M: 19[redacted] | NOT REPORTED |
| PRAVASTATIN | 80 mg | QD | Y-M: 19[redacted] | NOT REPORTED |
| MESALAZINE | 1000 mg | TID | Y-M: 20[redacted] | NOT REPORTED |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] | NOT REPORTED |
| ERGOCALCIFEROL | 2000 IU | QD | Y-M: 20[redacted] | NOT REPORTED |
| PREDNISONE | 1 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| IBANDRONIC ACID | 150 mg | OTHER: MONTHLY | Y-M: 20[redacted] | ONGOING |
| CLINDAMYCIN | 1 % | PRN | Y-M: 20[redacted] / 156 | NOT REPORTED |
| CYANOCOBALAMIN | 1000 mg/m2 | QD | Y-M: 20[redacted] / 567 | ONGOING |
| BIOTIN | 5000 mg | QD | Y-M: 20[redacted] / 616 | Y-M: 20[redacted] / 891 |
| AZITHROMYCIN | 500 mg | QD | Y-M: 20[redacted] / 856 | Y-M: 20[redacted] / 858 |
| CEFTRIAXONE | 1 g | QD | Y-M: 20[redacted] / 856 | Y-M: 20[redacted] / 858 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted] / 856 | Y-M: 20[redacted] / 858 |
| LACTULOSE | 20 g | PRN | Y-M: 20[redacted] / 856 | Y-M: 20[redacted] / 858 |

| | | | | |
|---|---|---|---|---|
| MACROGOL | 17 g | PRN | Y-M: 20[redacted] / 856 | Y-M: 20[redacted] / 858 |
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted] / 856 | Y-M: 20[redacted] / 858 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 856 | Y-M: 20[redacted] / 858 |
| SALBUTAMOL | 2.5 mg | PRN | Y-M: 20[redacted] / 856 | Y-M: 20[redacted] / 858 |
| LEVOFLOXACIN | 750 mg | QD | Y-M: 20[redacted] / 858 | Y-M: 20[redacted] / 862 |
| TRIAMCINOLONE | 0.1 % | BID | Y-M: 20[redacted] / 884 | NOT REPORTED |
| ULOBETASOL | 0.05 % | BID | Y-M: 20[redacted] / 884 | Y-M: 20[redacted] / 886 |

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

| | |
|---|---|
| **Event Description** | BACTERIAL PNEMONIA |
| **Preferred term** | 細菌性肺炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 851 |
| **Age at AE Onset** | 8[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 855): Chloride: 98 [95 - 108] MMOL/L; [redacted]20[redacted] (RX DAY 856): Alanine Aminotransferase: 67 [5 - 60] U/L; Albumin: 43 [34 - 49] G/L; Alkaline Phosphatase: 122 [40 - 140] U/L; Aspartate Aminotransferase: 40 [10 - 50] U/L; Bilirubin: 1 [0 - 2] UMOL/L; Blood Urea Nitrogen: 3.9 [2.9 - 8.9] MMOL/L; Calcium: 2.4 [2.2 - 2.59] MMOL/L; Chloride: 98 [95 - 108] MMOL/L; Creatinine: 74 [53 - 133] UMOL/L; Erythrocytes: 3.9 [4.3 - 6] 10^12/L; Glucose: 6.8 [3.9 - 6.4] MMOL/L; Hematocrit: 0.36 [0.4 - 0.53] FRACTION OF 1; Hemoglobin: 125 [135 - 170] G/L; Leukocytes: 6.2 [4 - 11] 10^9/L; Platelets: 177 [130 - 450] 10^9/L; Potassium: 3.8 [3.6 - 5.3] MMOL/L; Sodium: 136 [134 - 147] MMOL/L; [redacted]20[redacted] (RX DAY 857): Basophils/Leukocytes: 0 [0 - 0.2] %; Blood Urea Nitrogen: 4.3 [2.9 - 8.9] MMOL/L; Calcium: 2.25 [2.2 - 2.59] MMOL/L; Chloride: 97 [95 - 108] MMOL/L; Creatinine: 80 [53 - 133] UMOL/L; Eosinophils/Leukocytes: 0.1 [0 - 0.6] %; Erythrocytes: 3.6 [4.3 - 6] 10^12/L; Glucose: 6.7 [3.9 - 6.4] MMOL/L; Hematocrit: 0.35 [0.4 - 0.53] FRACTION OF 1; Hemoglobin: 116 [135 - 170] G/L; Leukocytes: 6.4 [4 - 11] 10^9/L; Lymphocytes/Leukocytes: 0.7 [0.9 - 3.9] %; Monocytes/Leukocytes: 1 [0.2 - 1] %; NPTST682-URINE TEST: NEGATIVE [NOT REPORTED - NOT REPORTED] 099,UNKNOWN; Neutrophils/Leukocytes: 4.4 [1.5 - 7.8] %; Platelets: 181 [130 - 450] 10^9/L; Potassium: 3.8 [3.6 - 5.3] MMOL/L; Sodium: 134 [134 - 147] MMOL/L; [redacted]20[redacted] (RX DAY 858): Calcium: 2.25 [2.2 - 2.59] MMOL/L; Creatinine: 75 [53 - 133] UMOL/L; Erythrocytes: 3.6 [4.3 - 6] 10^12/L; Glucose: 7 [3.9 - 6.4] MMOL/L; Hematocrit: 0.34 [0.4 - 0.53] FRACTION OF 1; Hemoglobin: 112 [135 - 170] G/L; Leukocytes: 6.5 [4 - 11] 10^9/L; Platelets: 206 [130 - 450] 10^9/L; Potassium: 4.1 [3.6 - 5.3] MMOL/L; Sodium: 134 [134 - 147] MMOL/L

**Microbiology**

[redacted]20[redacted] (RX DAY 856): BLOOD NPTST105-BLOOD CULTURE: Negative; OTHER NASAL NPTST196-COVID-19: Negative; [redacted]20[redacted](RX DAY 857): BLOOD NPTST524-PROCALCITONIN: Not applicable-5.84

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 856): CXR: FINDINGS CONCERNING WITH PNEUMONIA IN THE LEFT LUNG BASE. LIKELY ATELECTASIS RATHER THAN PNEUMONIA ON THE RIGHT

| | |
|---|---|
| **AE Stopped Rx Day** | 878 |
| **Duration of AE** | 28 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，細菌性肺炎の事象を発現した。

**Event 2 の臨床経過：**

関連する病歴は，元喫煙者（1 日 2 箱を 35 年間），うっ血性心不全，クローン病，局面型乾癬，乾癬性関節炎，ビタミン D 欠乏，骨粗鬆症及び飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は細菌性肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，細菌性肺炎は消失した。

被験者は，ゴルフをしているときに咳嗽と息切れが出現したと述べた。咳嗽はほぼ乾いており，副鼻腔からの少量の分泌物と咽頭痛が見られた。20[redacted] 年 [redacted] 月 [redacted] 日，1 週間で発熱，咳嗽及び息切れが悪化したと訴え入院した。胸痛，腹痛，悪心，嘔吐はないとのことであったが，便が緩くなったと訴えた。胸部 X 線の背腹像／側面像で左肺底部に肺炎の所見があり，右肺は肺炎というよりも無気肺の可能性が高かった。呼吸器感染症の診断におけるプロカルシトニンが上昇していた。被験者は，肺炎による頻呼吸と発熱を伴う急性敗血症を発現していた。被験者は静脈内投与及び呼吸療法で改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，polyethyiene glycol，levaquin，アジスロマイシン，zofran，アセトアミノフェン，albuterol，セフトリアキソン，エノキサパリン及びラクツロースであった。

**The patient's past medications include:**

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

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

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

PENICILLIN for UNKNOWN INDICATION

SULFA for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Pneumonia bacterial (10060946) (Pneumonia bacterial (10060946) ) [v.23.0] [10060946]

**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 BACTERIAL PNEUMONIA

**- Investigator:** Not applicable

**- AbbVie:** Risk factors include pre-existing congestive heartfailure, advanced age, and significant past smoking history of 70 pack years.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 67 no units

[redacted] **20[redacted] ALBUMIN:** 4.3 no units

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 122 No units

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 40 no units

[redacted] **20[redacted] BILIRUBIN:** 0.7 No units

[redacted] **20[redacted] BLOOD CULTURE:** Negative

[redacted] **20[redacted] CALCIUM:** 9.0 No units

[redacted] **20[redacted] CHEST X-RAY:** abnormal - possibility of anterior lobe bronchiectasis

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

[redacted] **20[redacted] CHLORIDE:** 98 No units

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

[redacted] **20[redacted] CREATININE:** 0.85 No units

[redacted] **20[redacted] CXR:** Findings concerning with Pneumonia in the left lung base. Likely atelectasis rather than pneumonia on the right

[redacted] **20[redacted] GLUCOSE:** 127 No units

[redacted] **20[redacted] HEMATOCRIT:** 36.3 No units

[redacted] **20[redacted] HEMATOCRIT:** 34.4 No units

[redacted] **20[redacted] HEMOGLOBIN:** 12.5 no units

[redacted] **20[redacted] HEMOGLOBIN:** 11.2 no units

[redacted] **20[redacted] PLATELET COUNT:** 177 No units

[redacted] **20[redacted] PLATELET COUNT:** 206 No units

[redacted] **20[redacted] POTASSIUM:** 4.1 no units

[redacted] **20[redacted] PROCALCITONIN:** 5.84 no units

[redacted] **20[redacted] RED BLOOD CELLS:** 3.85 no units

[redacted] **20[redacted] RED BLOOD CELLS:** 3.61 no units

[redacted] **20[redacted] SODIUM:** 134 no units

[redacted] **20[redacted] URINE:** Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 6.2 no units

[redacted] **20[redacted] WHITE BLOOD CELLS:** 6.5 no units

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 | | X |
| 深部静脈血栓症 | X | | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 30 mg QD | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| HYPERTENSION | NOT REPORTED |
| OTHER: NASAL ALLERGIES | 19[redacted] |
| OTHER: SEASONAL ALLERGIES | 19[redacted] |
| DIABETES MELLITUS: DIABETES | 20[redacted] |
| OTHER: HIGH LEVELS OF LDL | 20[redacted] |
| GASTROESOPHAGEAL REFLUX DISEASE: ACID REFULX | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: ESSENTIAL TREMOR | 20[redacted] |
| OTHER: ESSENTIAL TREMORS | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: FEMUR PLATE FROM CAR ACCIDENT | 20[redacted] |
| SURGERY: HEART CATHERIZATION | 20[redacted] |
| SURGERY: ESOPHAGUS STRETCH | 20[redacted] |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 169 | 169 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 170 | [redacted]20[redacted] / 386 | 217 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 387 | [redacted]20[redacted] / 452 | 66 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| FLUTICASONE | 50 OTHER: MCG | QD | Y-M: 19[redacted] |
| KETOTIFEN | 1 DROP PER EYE OTHER: 1 DROP PER EYE | QD | Y-M: 19[redacted] |
| LORATADINE | 10 mg | QD | Y-M: 19[redacted] |
| MONTELUKAST | 10 mg | QD | Y-M: 19[redacted] |
| ACETYLSALICYLIC ACID | 325 mg | QD | Y-M: 20[redacted] |
| DILTIAZEM | 240/24 mg | QD | Y-M: 20[redacted] |
| FISH OIL | 1200 IU | QD | Y-M: 20[redacted] |
| FUROSEMIDE | 20 mg | QD | Y-M: 20[redacted] |
| METFORMIN | 500 mg | BID | Y-M: 20[redacted] |
| NICOTINIC ACID | 1000 mg | QD | Y-M: 20[redacted] |
| SIMVASTATIN | 10 mg | QD | Y-M: 20[redacted] |
| UBIDECARENONE | 200 OTHER: MCG | QD | Y-M: 20[redacted] |
| VALSARTAN | 320 mg | QD | Y-M: 20[redacted] |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] |
| GLUCOSAMINE W/METHYLSULFONYLMETHANE | 1500 OTHER: MCG | QD | Y-M: 20[redacted] |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] |
| ZONISAMIDE | 100 mg | BID | Y-M: 20[redacted] |
| COLECALCIFEROL | 2000 IU | QD | Y-M: 20[redacted] |
| HERPES ZOSTER IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| DOCUSATE | 100 mg | QD | Y-M: 20[redacted] / -331 |

**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 |
|---|---|---|---|---|
| FLUTICASONE | 50 OTHER: MCG | QD | Y-M: 19[redacted] | ONGOING |
| KETOTIFEN | 1 DROP PER EYE OTHER: 1 DROP PER EYE | QD | Y-M: 19[redacted] | ONGOING |
| LORATADINE | 10 mg | QD | Y-M: 19[redacted] | ONGOING |
| MONTELUKAST | 10 mg | QD | Y-M: 19[redacted] | ONGOING |
| ACETYLSALICYLIC ACID | 325 mg | QD | Y-M: 20[redacted] | ONGOING |
| DILTIAZEM | 240/24 mg | QD | Y-M: 20[redacted] | ONGOING |
| FISH OIL | 1200 IU | QD | Y-M: 20[redacted] | ONGOING |
| FUROSEMIDE | 20 mg | QD | Y-M: 20[redacted] | ONGOING |
| METFORMIN | 500 mg | BID | Y-M: 20[redacted] | ONGOING |
| NICOTINIC ACID | 1000 mg | QD | Y-M: 20[redacted] | ONGOING |
| SIMVASTATIN | 10 mg | QD | Y-M: 20[redacted] | ONGOING |
| UBIDECARENONE | 200 OTHER: MCG | QD | Y-M: 20[redacted] | ONGOING |
| VALSARTAN | 320 mg | QD | Y-M: 20[redacted] | ONGOING |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] | ONGOING |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] | ONGOING |

| | | | | |
|---|---|---|---|---|
| GLUCOSAMINE W/METHYLSULFONYLMETHANE | 1500 OTHER: MCG | QD | Y-M: 20[redacted] | ONGOING |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] | ONGOING |
| ZONISAMIDE | 100 mg | BID | Y-M: 20[redacted] | ONGOING |
| COLECALCIFEROL | 2000 IU | QD | Y-M: 20[redacted] | ONGOING |
| DOCUSATE | 100 mg | QD | Y-M: 20[redacted] / -331 | ONGOING |
| PARACETAMOL | 650 mg | OTHER: Q4HR,PRN | Y-M: 20[redacted] / 452 | ONGOING |
| HEPARIN | 1 mL | OTHER: Q8HR | Y-M: 20[redacted] / 452 | Y-M: 20[redacted] / 452 |
| CEFTRIAXONE | 2 g | OTHER: Q24H | Y-M: 20[redacted] / 452 | Y-M: 20[redacted] / 477 |
| HYDRALAZINE | .5 mL | OTHER: Q4HR,PRN | Y-M: 20[redacted] / 452 | Y-M: 20[redacted] / 477 |
| MAGNESIUM HYDROXIDE | 30 mL | OTHER: DAILY, PRN | Y-M: 20[redacted] / 452 | Y-M: 20[redacted] / 477 |
| MORPHINE | 1 mL | OTHER: Q3HR, PRN | Y-M: 20[redacted] / 452 | Y-M: 20[redacted] / 477 |
| ONDANSETRON | 2 mL | OTHER: Q8HR,PRN | Y-M: 20[redacted] / 452 | Y-M: 20[redacted] / 477 |
| ONDANSETRON | 4 mg | OTHER: Q8HR, PRN | Y-M: 20[redacted] / 452 | Y-M: 20[redacted] / 477 |
| OXYCOCET | 1 OTHER: TAB | OTHER: Q4HR,PRN | Y-M: 20[redacted] / 452 | Y-M: 20[redacted] / 477 |
| VANCOMYCIN | 500 mL | OTHER: ONCE | Y-M: 20[redacted] / 452 | Y-M: 20[redacted] / 477 |
| CEFALEXIN | 500 mg | TID | Y-M: 20[redacted] / 477 | Y-M: 20[redacted] / 490 |
| RIVAROXABAN | 20 mg | OTHER: 1 TAB PO BID X 16 DAYS THEN PO, QD | Y-M: 20[redacted] / 477 | Y-M: 20[redacted] / 560 |

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

| | |
|---|---|
| **Event Description** | CELLULITIS LEFT LEG |
| **Preferred term** | 蜂巣炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 452 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 452): Blood Urea Nitrogen: 8.6 [2.5 - 6.4] MMOL/L; Calcium: 2.25 [2.12 - 2.52] MMOL/L; Chloride: 104 [98 - 107] MMOL/L; Creatinine: 133 [53 - 115] UMOL/L; Erythrocytes: 4 [4 - 5.4] 10^12/L; Glucose: 5.6 [3.9 - 5.5] MMOL/L; Hematocrit: 0.4 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 136 [140 - 180] G/L; Leukocytes: 14.6 [4.2 - 10.8] 10^9/L; NPTST045-ANION GAP, BLOOD: 7 [5 - 15] MMOL/L; NPTST092-BASOPHIL AUTO: 0.1 [0 - 3] %; NPTST178-CO2 LAB: 26 [21 - 32] MMOL/L; NPTST362-IG% AUTO: 0.9 [0 - 0.4] %; NPTST402-LACTIC ACID: 2.3 [0.4 - 2] MMOL/L; NPTST418-LYMPH AUTO: 6.3 [24 - 44] %; NPTST427-MCH: 34.3 [25.4 - 34.6] PG; NPTST428-MCHC: 33.8 [31 - 37] GM/DL; NPTST429-MCV: 102 [80 - 99] FL; NPTST451-MONO AUTO: 4 [0 - 15] %; NPTST454-MPV: 9.2 [7 - 14] FL; NPTST468-NEUTRO AUTO: 88.7 [41 - 77] %; NPTST541-PT: 14.2 [11.5 - 14.6] SEC; NPTST562-RDW: 15.1 [11.5 - 14.5] %; Neutrophils: 12.99 [1.8 - 7] 10^9/L; Platelets: 304 [130 - 450] 10^9/L; Potassium: 3.5 [3.5 - 5.1] MMOL/L; Prothrombin Intl. Normalized Ratio: 1.1 [0.8 - 1.2] RATIO; Sodium: 137 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 453): NPTST402-LACTIC ACID: 0.9 [0.4 - 2] MMOL/L; [redacted]20[redacted] (RX DAY 476): Blood Urea Nitrogen: 2.5 [2.5 - 6.4] MMOL/L; Calcium: 2.35 [2.12 - 2.52] MMOL/L; Chloride: 104 [98 - 107] MMOL/L; Glucose: 7.3 [3.9 - 5.5] MMOL/L; Hematocrit: 0.3 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 95 [140 - 180] G/L; Leukocytes: 9.7 [4.2 - 10.8]

10^9/L; NPTST422-MAGNESIUM: 2 [1.8 - 2.4] MG/DL; NPTST511-PHOSPHORUS: 3.4 [2.5 - 4.9] MG/DL; Platelets: 521 [130 - 450] 10^9/L; Potassium: 3.7 [3.5 - 5.1] MMOL/L; Sodium: 136 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 477): Creatinine: 88 [53 - 115] UMOL/L

**Microbiology**

[redacted]20[redacted](RX DAY 453): OTHER BLOOD CULTURES NPTST270-FILMARRAY BCID: Positive-STAPHYLOCOCCUS AUREUS

**SAE Supplemental Procedure**

[redacted]20[redacted](RX DAY 452): VENOUS DOPPLER ULTRASOUND- LEFT LOWER EXTREMITY: NORMAL VENOUS DOPPLER ULTRASOUND OF THE LOWER EXTREMITY; [redacted]20[redacted] (RX DAY 455): ARTERIAL DOPPLER ULTRASOUND- LEFT LOWER EXTREMITY: APPROXIMATELY 30% STENOSIS IS AT THE LEVEL OF THE LEFT PROXIMAL SUPERFICIAL FEMORAL ARTERY. NO OTHER EVIDENCE OF SIGNIFICANT LEFT LOWER EXTREMITY ARTERIAL STENOTIC OR ARTERIAL OCCLUSIVE DISEASE OF THE LEFT LOWER EXTREMITY. MONOPHASIC FLOW WITH IN THE POPLITEAL AND TRIFURCATION CYST OF THE LEFT LOWER EXTREMITIES CONSISTENT WITH MARKED ARTERIAL DISEASE. CTA LOWER EXTREMITIES SHOULD BE OBTAINED FOR FURTHER EVALUATION.; [redacted]20[redacted] (RX DAY 456): CT BRAIN WITHOUT CONTRAST: NO ACUTE INTRACRANIAL ABNORMALITY VISUALIZED; [redacted]20[redacted] (RX DAY 459): CT LEFT TIBIA AND FIBULA: CELLULITIS IN THE LEFT SHIN AND FOOT. NO FLUID COLLECTION. NO FRACTURE OR DISLOCATION IN THE LEFT TIBIA OR FIBULA. NO EVIDENCE OF OSTEOMYELITIS. QUESTIONABLE NON OCCLUSIVE THROMBUS IN THE PERONEALVEIN. FURTHER EVALUATION WITH ULTRASOUND IS RECOMMENDED.; VENOUS DOPPLER ULTRASOUND- LEFT LOWER EXTREMITY: FINDINGS ARE POSITIVE FOR DISTENDED PERONEAL VEIN WITH OCCLUSIVE THROMBUS WITHOUT COMPRESSION OR COLOR FLOW. GIVEN THE LIMITED COMPRESSION OF THE VESSELS RECOMMEND SHORT-TERM INTERVAL FOLLOW-UP STUDY.THE POSTERIOR TIBIAL VEIN DEMONSTRATE COLOR FLOW APPEARS TO BE PATENT. THERE IS CALF EDEMA.; [redacted]20[redacted] (RX DAY 466): 4 COMPARTMENT FASCIOTOMY LEFT LEG: REMOVAL OF DEEP FOREIGN BODY LEFT LEG

| | |
|---|---|
| **AE Stopped Rx Day** | 506 (54 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 55 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

**Event #2: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events**

| | |
|---|---|
| **Event Description** | DEEP VEIN THROMBOSIS LEFT LEG |
| **Preferred term** | 深部静脈血栓症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 459 (7 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 452): Blood Urea Nitrogen: 8.6 [2.5 - 6.4] MMOL/L; Calcium: 2.25 [2.12 - 2.52] MMOL/L; Chloride: 104 [98 - 107] MMOL/L; Creatinine: 133 [53 - 115] UMOL/L; Erythrocytes: 4 [4 - 5.4] 10^12/L; Glucose: 5.6 [3.9 - 5.5] MMOL/L; Hematocrit: 0.4 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 136 [140 - 180] G/L; Leukocytes: 14.6 [4.2 - 10.8] 10^9/L; NPTST045-ANION GAP, BLOOD: 7 [5 - 15] MMOL/L; NPTST092-BASOPHIL AUTO: 0.1 [0 - 3] %; NPTST178-CO2 LAB: 26 [21 - 32] MMOL/L; NPTST362-IG% AUTO: 0.9 [0 - 0.4] %; NPTST402-LACTIC ACID: 2.3 [0.4 - 2] MMOL/L; NPTST418-LYMPH AUTO: 6.3 [24 - 44] %; NPTST427-MCH: 34.3 [25.4 - 34.6] PG; NPTST428-MCHC: 33.8 [31 - 37] GM/DL; NPTST429-MCV: 102 [80 - 99] FL; NPTST451-MONO AUTO: 4 [0 - 15] %; NPTST454-MPV: 9.2 [7 - 14] FL; NPTST468-NEUTRO AUTO: 88.7 [41 - 77] %; NPTST541-PT: 14.2 [11.5 - 14.6] SEC; NPTST562-RDW: 15.1 [11.5 - 14.5] %; Neutrophils: 12.99 [1.8 - 7] 10^9/L; Platelets: 304 [130 - 450] 10^9/L; Potassium: 3.5 [3.5 - 5.1] MMOL/L; Prothrombin Intl. Normalized Ratio: 1.1 [0.8 - 1.2] RATIO; Sodium: 137 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 453): NPTST402-LACTIC ACID: 0.9 [0.4 - 2] MMOL/L; [redacted]20[redacted] (RX DAY 476): Blood Urea Nitrogen: 2.5 [2.5 - 6.4] MMOL/L; Calcium: 2.35 [2.12 - 2.52] MMOL/L; Chloride: 104 [98 - 107] MMOL/L; Glucose: 7.3 [3.9 - 5.5] MMOL/L; Hematocrit: 0.3 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 95 [140 - 180] G/L; Leukocytes: 9.7 [4.2 - 10.8] 10^9/L; NPTST422-MAGNESIUM: 2 [1.8 - 2.4] MG/DL; NPTST511-PHOSPHORUS: 3.4 [2.5 - 4.9] MG/DL; Platelets:

521 [130 - 450] 10^9/L; Potassium: 3.7 [3.5 - 5.1] MMOL/L; Sodium: 136 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 477): Creatinine: 88 [53 - 115] UMOL/L

**Microbiology**

[redacted]20[redacted] (RX DAY 453): OTHER BLOOD CULTURES NPTST270-FILMARRAY BCID: Positive-STAPHYLOCOCCUS AUREUS

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 452): VENOUS DOPPLER ULTRASOUND- LEFT LOWER EXTREMITY: NORMAL VENOUS DOPPLER ULTRASOUND OF THE LOWER EXTREMITY; [redacted]20[redacted] (RX DAY 455): ARTERIAL DOPPLER ULTRASOUND- LEFT LOWER EXTREMITY: APPROXIMATELY 30% STENOSIS IS AT THE LEVEL OF THE LEFT PROXIMAL SUPERFICIAL FEMORAL ARTERY. NO OTHER EVIDENCE OF SIGNIFICANT LEFT LOWER EXTREMITY ARTERIAL STENOTIC OR ARTERIAL OCCLUSIVE DISEASE OF THE LEFT LOWER EXTREMITY. MONOPHASIC FLOW WITH IN THE POPLITEAL AND TRIFURCATION CYST OF THE LEFT LOWER EXTREMITIES CONSISTENT WITH MARKED ARTERIAL DISEASE. CTA LOWER EXTREMITIES SHOULD BE OBTAINED FOR FURTHER EVALUATION.; [redacted]20[redacted] (RX DAY 456): CT BRAIN WITHOUT CONTRAST: NO ACUTE INTRACRANIAL ABNORMALITY VISUALIZED; [redacted]20[redacted] (RX DAY 459): CT LEFT TIBIA AND FIBULA: CELLULITIS IN THE LEFT SHIN AND FOOT. NO FLUID COLLECTION. NO FRACTURE OR DISLOCATION IN THE LEFT TIBIA OR FIBULA. NO EVIDENCE OF OSTEOMYELITIS. QUESTIONABLE NON OCCLUSIVE THROMBUS IN THE PERONEALVEIN. FURTHER EVALUATION WITH ULTRASOUND IS RECOMMENDED.; VENOUS DOPPLER ULTRASOUND- LEFT LOWER EXTREMITY: FINDINGS ARE POSITIVE FOR DISTENDED PERONEAL VEIN WITH OCCLUSIVE THROMBUS WITHOUT COMPRESSION OR COLOR FLOW. GIVEN THE LIMITED COMPRESSION OF THE VESSELS RECOMMEND SHORT-TERM INTERVAL FOLLOW-UP STUDY.THE POSTERIOR TIBIAL VEIN DEMONSTRATE COLOR FLOW APPEARS TO BE PATENT. THERE IS CALF EDEMA.; [redacted]20[redacted] (RX DAY 466): 4 COMPARTMENT FASCIOTOMY LEFT LEG: REMOVAL OF DEEP FOREIGN BODY LEFT LEG

| | |
|---|---|
| **AE Stopped Rx Day** | 560 (108 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 102 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | PROLONGED HOSPITALIZATION FOR CELLULITIS |
| **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:** M15-572

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，左脚蜂巣炎及び左脚深部静脈血栓症の事象を発現した。

**Event 1 及び 2 の臨床経過：**

関連する病歴は，糖尿病，LDL 高値，乾癬性関節炎，局面型乾癬，高血圧，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左脚蜂巣炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左脚深部静脈血栓症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左脚蜂巣炎は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，左脚深部静脈血栓症は消失した。

本事象発現の 1 週間前，被験者は穴に落ちて左膝を受傷した。被験者の報告では，頭部損傷や意識消失はなかったが，体重をかけると疼痛が増強し，歩行困難で杖が必要であった。被験者は温湿布，タイレノール，Aleve により自身で治療を行った。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は疼痛の増強（10/10）及び下腿全体の腫脹，並びに 103°F の発熱を伴う悪寒を報告した。また，温湿布を長時間貼りすぎて皮膚に赤色の発疹が出たとのことであった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は診察のため救急診療所（urgent care）を受診した。血液検査報告で白血球数増加が認められた。ロセフィン 2 g が筋肉内投与され，精査のため救急治療室に搬送された。被験者は SIRS／早期敗血症の基準を満たし，抗生物質の静脈内投与が開始された。同日，被験者は左下肢蜂巣炎及び MSSA（メチシリン感受性黄色ブドウ球菌）菌血症のため入院した。血液培養では黄色ブドウ球菌が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は下肢動脈ドップラー検査を受け，左近位浅大腿動脈に約 30%の狭窄が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左下肢静脈ドップラー検査を受け，閉塞性血栓による腓骨静脈の拡張が認められ，抗凝固療法が開始された。臨床的改善が見られず，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 4 区画筋膜切開術を受け，左下肢の深部異物が除去された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は創部陰圧療法を受けた状態で退院した。

治験責任医師によると，本事象に関連する被験者の危険因子は病歴及び肥満と考えられた。

**病院記録より：**

被験者の下肢は浮腫と紅斑が著明であり，触れると温感と疼痛が認められた。

左脚蜂巣炎の事象により治験薬の投与が完全に中止された。

投与された薬剤は，タイレノール，バンコマイシン，aleve，ロセフィン，percocet，モルヒネ，cephalexin 及びリバーロキサバンであった。

**The patient's past medications include:**

TETRACYCLINE for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Cellulitis of leg (10007912) (Cellulitis (10007882) ) [v.23.0] [10007912]

**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) Thrombosis of leg deep venous (10043630) (Deep vein thrombosis (10051055) ) [v.23.0] [10043630]

**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)

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Event of CELLULITIS LEFT LEG

**- Investigator:** Not applicable.

**- AbbVie:** Risk factors include injury to left knee and falling into a hole, rash on left leg after leaving heating pad on too long, pre-existing diabetes and obesity.

Event of DEEP VEIN THROMBOSIS LEFT LEG

**- Investigator:** PROLONGED HOSPITALIZATION FOR CELLULITIS

**- AbbVie:** Risk factors include trauma to left leg, prolonged hospitalization, and obesity

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ARTERIAL DOPPLER:** Left lower extremity - approximately 30% stenosis is at the level of the left proximal superficial femoral artery. No other evidence of significant left lower extremity arterial stenotic or arterial occlusive disease of the left lower extremity. Monophasic flow with in the popliteal and trifurcation cyst of the left lower extremities consistent with marked arterial disease. CTA lower extremities should be obtained for further evaluation.

[redacted] **20[redacted] BLOOD CULTURE:** positive for Staphylococcus aureus

[redacted] **20[redacted] BMI:** 42.6 kg/m**2

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

[redacted] **20[redacted] BUN:** 24 mg/dL (normal 7 to 18)

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

[redacted] **20[redacted] CT BRAIN WITHOUT CONTRAST:** No acute intracranial abnormality visualized

[redacted] **20[redacted] CT LEFT TIBIA AND FIBULA:** Cellulitis in the left shin and foot. No fluid collection. No fracture or dislocation in the left tibia or fibula. No evidence of osteomyelitis. Questionable non occlusive thrombus in the peroneal vein. Further evaluation with ultrasound is recommended.

[redacted] **20[redacted] GLUCOSE:** 132 mg/dL (normal 70 to 99)

[redacted] **20[redacted] HEMATOCRIT:** 40.2 % (normal 42 to 52)

[redacted] **20[redacted] HEMATOCRIT:** 30.3 % (normal 42 to 52)

[redacted] **20[redacted] HEMOGLOBIN:** 13.6 G/DL (normal 14 to 18)

[redacted] **20[redacted] HEMOGLOBIN:** 9.5 G/DL (normal 14 to 18)

[redacted] **20[redacted] IG PERCENT:** 0.9 % (normal 0 to 0.4)

[redacted] **20[redacted] INR:** 1.1 ratio (normal 0.8 to 1.2)

[redacted] **20[redacted] LACTIC ACID:** 2.3 no units

[redacted] **20[redacted] LYMPHOCYTES:** 6.3 % (normal 24 to 44)

[redacted] **20[redacted] MONOCYTES:** 4 % (normal 0 to 15)

[redacted] **20[redacted] NEUTROPHILS:** 88.7 % (normal 41 to 77)

[redacted] **20[redacted] NEUTROPHILS ABS:** 12.9 TH/UL (normal 1.8 to 7)

[redacted] **20[redacted] PLATELET COUNT:** 304 TH/UL (normal 150 to 450)

[redacted] **20[redacted] PLATELET COUNT:** 521 TH/UL (normal 150 to 450)

[redacted] **20[redacted] PROCALCITONIN:** 0.89 no units

[redacted] **20[redacted] PT:** 14.2 SEC (normal 11.5 to 14.6)

[redacted] **20[redacted] VENOUS DOPPLER:** Left lower extremity - normal venous Doppler ultrasound of the lower extremity

[redacted] **20[redacted] VENOUS DOPPLER:** Left lower extremity - findings are positive for distended peroneal vein with occlusive thrombus without compression or color flow. given the limited compression of the vessels recommend short-term interval follow-up study. The posterior tibial vein demonstrate color flow appears to be patent. There is calf edema.

[redacted] **20[redacted] WBC:** 14.6 TH/UL (normal 4.2 to 10.8)

[redacted] **20[redacted] WBC:** 9.7 TH/UL (normal 4.2 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 |
|---|---|---|---|---|
| 心停止 | X | | X | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 30 mg QD | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| HYPERTENSION | 19[redacted] |
| HYPOTHYROIDISM | 19[redacted] |
| HYPERLIPIDEMIA | 19[redacted] |
| OSTEOARTHRITIS | 20[redacted] |
| DIABETES MELLITUS | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: TONSILECTOMY | 19[redacted] |
| SURGERY: VASECTOMY | 19[redacted] |
| SURGERY: RIGHT WRIST REPAIR | 20[redacted] |
| SURGERY: RIGHT SHOULDER REPAIR | 20[redacted] |
| SURGERY: RIGHT SHOULDER LIGAMENT RETRACTION REPAIR | 20[redacted] |
| SURGERY: RIGHT WRIST CARPAL TUNNEL RELEASE | 20[redacted] |
| SURGERY: RIGHT WRIST FUSION | 20[redacted] |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 56 | 56 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| DILTIAZEM | 240 mg | QD | Y-M: 19[redacted] |
| ENALAPRIL | 10 mg | QD | Y-M: 19[redacted] |
| LEVOTHYROXINE | 275 ug | QD | Y-M: 19[redacted] |
| LOVASTATIN | 20 mg | QD | Y-M: 19[redacted] |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 19[redacted] |
| OXYCOCET | 75 mg | BID | Y-M: 20[redacted] |
| PARACETAMOL | 325 mg | BID | Y-M: 20[redacted] |
| GLIPIZIDE | 10 mg | QD | Y-M: 20[redacted] |
| METFORMIN | 1000 mg | QD | Y-M: 20[redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -292 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -292 |

**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 |
|---|---|---|---|---|
| DILTIAZEM | 240 mg | QD | Y-M: 19[redacted] | Y-M: 20[redacted] / 62 |
| ENALAPRIL | 10 mg | QD | Y-M: 19[redacted] | Y-M: 20[redacted] / 62 |
| LEVOTHYROXINE | 275 ug | QD | Y-M: 19[redacted] | Y-M: 20[redacted] / 62 |
| LOVASTATIN | 20 mg | QD | Y-M: 19[redacted] | Y-M: 20[redacted] / 62 |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 19[redacted] | Y-M: 20[redacted] / 62 |
| GLIPIZIDE | 10 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 62 |
| METFORMIN | 1000 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 62 |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -292 | Y-M: 20[redacted] / 62 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -292 | Y-M: 20[redacted] / 62 |

**Event #1: Serious Adverse Event, Death, Event of Interest - Adjudicated Cardiovascular Events**

| | |
|---|---|
| **Event Description** | CARDIAC ARREST |
| **Preferred term** | 心停止 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 62 (6 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **SAE Supplemental Procedure** | |
| NOT REPORTED | |
| **AE Stopped Rx Day** | 62 (6 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 1 DAY |
| **Severity** | Mild |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | DIABETES, HYPERLIPIDEMIA, HYPERTENSION |
| **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:** M15-572

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，致死的な心停止の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，高血圧，甲状腺機能低下症，高脂血症，糖尿病，乾癬性関節炎及び非喫煙者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年[redacted] 月[redacted] 日であった。

20[redacted] 年[redacted] 月[redacted] 日，被験者は心停止を発現した。20[redacted] 年[redacted] 月[redacted] 日，被験者は死亡した。死因は心停止と報告された。剖検は実施されなかった。

被験者は運転中に詳細不明の緊急事態に陥り，死亡した。治験責任医師による追加情報の入手は不可である。

死亡診断書は入手されなかった。

Causality for UPADACITINIB (Blinded)

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1) Cardiac arrest (10007515) (Cardiac arrest (10007515) ) [v.22.1] [10007515]

**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)

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Event of CARDIAC ARREST

**- Investigator:** Diabetes, hyperlipidemia, and hypertension.

**- AbbVie:** Event is more likely related to preexisting diabetes mellitus, hypertension, hyperlipidemia and obesity

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 |
| 虚血性脳卒中 | X | | | X |

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

| Medical History | Onset Year |
|---|---|
| TUBERCULOSIS: LATENT TB | 19[redacted] |
| CORONARY ARTERY DISEASE | 19[redacted] |
| HYPERTENSION | 19[redacted] |
| DIABETES MELLITUS | 20[redacted] |
| OTHER: JOINTS PAIN/ARTHRITIS | 20[redacted] |
| HYPERLIPIDEMIA: HIGH CHOLESTEROL | 20[redacted] |
| BENIGN PROSTATIC HYPERPLASIA: PROSTATIC HYPERTROPHY | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: RIGHT AND LEFT EYE GLAUCOMA | 20[redacted] |
| OTHER: URINARY RETENTION | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: TONSILLECTOMY | 19[redacted] |
| SURGERY: APPENDECTOMY | 19[redacted] |
| SURGERY: CORONARY BYPASS | 19[redacted] |
| SURGERY: RENAL ARTERY STENT | 20[redacted] |
| SURGERY: LEG VEIN ABLATION | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1.5 PACK | 25 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 1 | [redacted] / 168 | 168 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 169 | [redacted] / 393 | 225 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] 2019 / 394 | [redacted] / 682 | 289 |

**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: 19[redacted] |
| ALLOPURINOL | 300 mg | QD | Y-M: 20[redacted] |
| CHONDROITIN | 300 mg | QD | Y-M: 20[redacted] |
| GLUCOSAMINE | 300 mg | QD | Y-M: 20[redacted] |
| METFORMIN | 500 mg | QD | Y-M: 20[redacted] |
| AMLODIPINE | 5 mg | QD | Y-M: 20[redacted] |
| ATORVASTATIN | 80 mg | QD | Y-M: 20[redacted] |
| CARVEDILOL | 12.5 mg | BID | Y-M: 20[redacted] |
| ISOSORBIDE MONONITRATE | 30 mg | QD | Y-M: 20[redacted] |
| METHOTREXATE | 20 mg | QD | Y-M: 20[redacted] |
| LOSARTAN | 25 mg | QD | Y-M: 20[redacted] |
| TAMSULOSIN | 4 mg | QD | Y-M: 20[redacted] / -233 |

**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: 19[redacted] | ONGOING |
| ALLOPURINOL | 300 mg | QD | Y-M: 20[redacted] | ONGOING |
| CHONDROITIN | 300 mg | QD | Y-M: 20[redacted] | ONGOING |
| GLUCOSAMINE | 300 mg | QD | Y-M: 20[redacted] | ONGOING |
| METFORMIN | 500 mg | QD | Y-M: 20[redacted] | ONGOING |
| AMLODIPINE | 5 mg | QD | Y-M: 20[redacted] | ONGOING |
| ATORVASTATIN | 80 mg | QD | Y-M: 20[redacted] | ONGOING |
| CARVEDILOL | 12.5 mg | BID | Y-M: 20[redacted] | ONGOING |
| ISOSORBIDE MONONITRATE | 30 mg | QD | Y-M: 20[redacted] | ONGOING |
| METHOTREXATE | 20 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 454 |
| LOSARTAN | 25 mg | QD | Y-M: 20[redacted] | ONGOING |
| TAMSULOSIN | 4 mg | QD | Y-M: 20[redacted] / -233 | ONGOING |
| CLOPIDOGREL | 75 mg | QD | Y-M: 20[redacted] / 309 | ONGOING |
| IRON | 324 mg | QD | Y-M: 20[redacted] / 310 | ONGOING |
| SALBUTAMOL | 90 OTHER: MCG | PRN | Y-M: 20[redacted] / 462 | ONGOING |
| CEFALEXIN | 1 g | QD | Y-M: 20[redacted] / 462 | Y-M: 20[redacted] / 464 |
| DOXYCYCLINE | 100 mg | BID | Y-M: 20[redacted] / 474 | Y-M: 20[redacted] / 481 |

**Event #1: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events**

| | |
|---|---|
| **Event Description** | ISCHEMIC CEREBRAL VASCULAR ACCIDENT |
| **Preferred term** | 虚血性脳卒中 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 306 |
| **Age at AE Onset** | 7[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 306): Basophils: 0.02 [0 - 0.1] 10^9/L; Eosinophils: 0.03 [0.04 - 0.35] 10^9/L; Erythrocytes: 3.7 [4.4 - 5.6] 10^12/L; Hematocrit: 0.38 [0.4 - 0.5] FRACTION OF 1; Leukocytes: 4.9 [4.5 - 10] 10^9/L; Monocytes: 0.58 [0.2 - 1] 10^9/L; NPTST320-HEMOGLOBIN: 11.9 [13 - 17] G/DL; [redacted]20[redacted] (RX DAY 671): Lymphocytes: 0.82 [0.9 - 5] 10^9/L; Neutrophils: 3.35 [1.8 - 7.7] 10^9/L

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 306): MRI BRAIN: ISCHEMIC CVA; [redacted]20[redacted] (RX DAY 308): MRI OF THE BRAIN: HIGH GRADE RIGHT VERTEBRAL ARTERY STENOSIS,LEFT HEMISPHERIC STROKE, MODERATE CAROTID STENOSIS; TRANSTHORACIC ECHO: MITRAL VALVE SCLEROSIS, MILD-MODERATE MITRAL REGURGITATION,TRICAFLCT AORTIC VLAVE WITH SCLEROSIS, TRACE PULMONARY VALVE REGURGITATION; [redacted]20[redacted] (RX DAY 309): CT ANGIOGRAM OF HEAD AND NECK: CT ANGIOGRAM OF THE HEAD AND NECK REVEALED FOCAL STENOSIS OF THE RIGHT VERTEBRAL ARTERYOF 80% AND 60% NARROWING OF LEFT INTERNAL CAROTID ARTERY.; CT BRAIN: CT SCAN OF BRAIN WAS PERFORMED AND WAS NEGATIVE.; [redacted]20[redacted] (RX DAY 344): CT SCAN HEAD: MILD TO MODERATE GENERALIZED VOLUME LOSS AND MILD CHRONIC WHITE MATTER ISCHEMIA

| | |
|---|---|
| **AE Stopped Rx Day** | 344 |
| **Duration of AE** | 39 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | CORONARY ARTERY DISEASE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

**Event #3: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | BRONCHITIS |
| **Preferred term** | 気管支炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 460 |
| **Age at AE Onset** | 7[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Rx Day** | 481 |
| **Duration of AE** | 22 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | SUBJECT WAS OUT OF THE COUNTRY AND BY AGE HE WAS MAY LIABLE TO DIFFERENT TYPES OF 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:** M15-572

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，虚血性脳血管発作の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，元喫煙者（1 日 1.5 箱を 25 年間），冠動脈疾患，高血圧，冠動脈バイパス，腎動脈ステント，糖尿病，コレステロール高値，乾癬性関節炎及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。記録によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は虚血性脳血管発作を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，虚血性脳血管発作は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右側の脱力及び顔面・腕のしびれ感で入院した。被験者は意識清明で，人・場所・時間の見当識障害はなく，発話・言語・理解力も正常であった。右上肢にごくわずかな脱力があり，靴下・手袋型分布における軽度の感覚低下を伴っていた。振戦は見られなかった。被験者は右側の顔面・腕の運動／感覚消失を呈していた。被験者によると，失語症，嚥下障害，構語障害，回転性めまい，霧視，運動失調，眼振，複視，錯乱，意識消失／低下及び四肢の運動／感覚消失はなかった。脳 MRI 検査及び頭部 CT 検査の結果，虚血性脳血管発作と診断された。被験者は，障害や長期に及ぶ後遺症なく回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

医療記録によると，被験者は，前の週に出現した 1 日間の右側しびれ感のため，20[redacted] 年 [redacted] 月 [redacted] 日に脳 MRI 検査，20[redacted] 年 [redacted] 月 [redacted] 日に腰椎 MRI 検査を受けた。脳 MRI 検査の結果，急性梗塞，頭蓋内出血及び腫瘤の影響は認められず，軽度から中等度の脳全体の容積減少及び軽度の慢性白質虚血が認められた。腰椎所見は，軽度の脊椎症性変形，局所的な椎間板ヘルニア及び

狭窄なし，真性神経根圧迫なしであった。

投与された薬剤は，硫酸鉄，プラビックス及びアスピリンであった。

Causality for UPADACITINIB (Blinded)

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1) Ischaemic stroke (10061256) (Ischaemic stroke (10061256) ) [v.22.1] [10061256]

**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 ISCHEMIC CEREBRAL VASCULAR ACCIDENT

**- Investigator:** CORONARY ARTERY DISEASE

**- AbbVie:** EVENT IS MORE LIKELY RELATED TO ADVANCED AGE, PRE-EXISTING DIABETES MELLITUS, HYPERTENSION AND HIGH CHOLESTEROL.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] ANGIOGRAM:** CT ANGIOGRAM OF HEAD AND NECK: Significant focal stenosis of the right vertebral artery of 80% and 60%narrowing of the left internal carotid artery.

[redacted] **20[redacted] BLOOD PRESSURE:** 176/62 mmHg

[redacted] **20[redacted] BODY TEMPERATURE:** 37.9 Degrees C

[redacted] **20[redacted] CT BRAIN:** ischemic CVA

[redacted] **20[redacted] CT HEAD:** ischemic CVA

[redacted] **20[redacted] CT HEAD:** Mild to moderate generalized volume loss and mild chronic white matter ischemia

[redacted] 20[redacted] **HBA1C:** 6.1

[redacted] 20[redacted] **HEART RATE:** 64 /min

[redacted] 20[redacted] **LDL:** 37 mg/dL

[redacted] 20[redacted] **MRI BRAIN:** ischemic CVA

[redacted] 20[redacted] **MRI BRAIN:** high grade right vertebral artery stenosis, left hemispheric stroke, moderate carotid stenosis

[redacted] 20[redacted] **MRI BRAIN WITHOUT CONTRAST:** IMPRESSION: No acute infarct, intracranial hemorrhage or mass effect. Mild to moderate generalized volume loss and mild chronic white matter ischemia.

[redacted] 20[redacted] **MRI LUMBAR SPINE WITHOUT CONTRAST:** IMPRESSION: Mild spondylotic changes. No focal disc herniation or stenosis. No frank nerve root compression.

[redacted] 20[redacted] **RESPIRATORY RATE:** 18 /min

[redacted] 20[redacted] **TRIGLYCERIDES:** 322 mg/dL

[redacted] 20[redacted] **TTE:** IMPRESSION: Lumason was used; NO PERICARDIAL EFFUSION; LEFT VENTRICLE EF is estimated at 50% to 55%; MITRAL VALVE sclerosis, mild-moderate regurgitation; TRILEAFLET AORTIC VALVE with sclerosis, no regurgitation; RIGHT ATRIUM mildly increased right atrial size; RIGHT VENTRICLE mildly increased size with systolic pressure of 24.9mmHg; TRICUSPID VALVE trace to mild regurgitation; PULMONARY VALVE trace regurgitation; INTER-ATRIAL SHUNTING
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，気管支炎の事象を発現した。

**Event 3 の臨床経過：**

関連する病歴は，結核（非活動性結核），元喫煙者（1 日 1.5 箱を 25 年間），高血圧，糖尿病，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。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

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

本事象発現前，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は慢性腎臓病（非重篤な事象）を発現し，治験薬の投与が休止された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は咳嗽及び発熱で入院した。治験責任医師によると，本事象に関連する危険因子は被験者の年齢であった。投与された薬剤は抗生物質であり，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，セファレキシン，ドキシサイクリン及び pro-air であった。

Causality for UPADACITINIB (Blinded)

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1) Bronchitis (10006451) (Bronchitis (10006451) ) [v.22.1] [10006451]

**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 BRONCHITIS

**- Investigator:** Unknown

**- AbbVie:** Event is common in the general population.

Relevant Laboratory & Other Diagnostic Tests

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

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

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 |
|---|---|---|---|---|
| 卵管嚢胞 | X | | | |
| 出血性卵巣嚢胞 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 15 mg QD | 4[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| MIGRAINE HEADACHE | 19[redacted] |
| OTHER: PLAGUE PSORIASIS | 19[redacted] |
| OTHER: ALLERGIC TO BEES | 20[redacted] |
| DEPRESSION | 20[redacted] |
| CEREBRAL VASCULAR ACCIDENT: STROKE | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| SEIZURE DISORDER/CONVULSIONS: SEIZURE | 20[redacted] |
| GASTROESOPHAGEAL REFLUX DISEASE: ACID REFLUX | 20[redacted] |
| OTHER: NAUSEA | 20[redacted] |
| OTHER: HIGH CHOLESTEROL | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| Not reported. | |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | CURRENT | 1 PACK | 25 | |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 166 | 166 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 167 | [redacted]20[redacted] / 391 | 225 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 392 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| SALBUTAMOL | 90 gtt | PRN | Y-M: 20[redacted] |
| ALPRAZOLAM | 0.5 mg | QD | Y-M: 20[redacted] |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] |
| TRAZODONE | 100 mg | QD | Y-M: 20[redacted] |
| AXOTAL | 25 mg | PRN | Y-M: 20[redacted] |
| SUMATRIPTAN | 100 mg | PRN | Y-M: 20[redacted] |
| ACETYLSALICYLIC ACID | 325 mg | QD | Y-M: 20[redacted] |
| ZESTORETIC | 12.5 mg | QD | Y-M: 20[redacted] |
| LEVETIRACETAM | 750 mg | QD | Y-M: 20[redacted] |
| BETAMETHASONE | 0.05 % | BID | Y-M: 20[redacted] |
| CLOBETASOL | 0.05 % | PRN | Y-M: 20[redacted] |
| OMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted] |
| PROMETHAZINE | 25 mg | QD | Y-M: 20[redacted] |
| TRIAMCINOLONE | 0.5 % | BID | Y-M: 20[redacted] |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] / -194 |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -149 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -149 |
| METHYLPREDNISOLONE | 40 mg | OTHER: ONE TIME | Y-M: 20[redacted] / -90 |

**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 | 90 gtt | PRN | Y-M: 20[redacted] | NOT REPORTED |
| ALPRAZOLAM | 0.5 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| TRAZODONE | 100 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| AXOTAL | 25 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| SUMATRIPTAN | 100 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| ACETYLSALICYLIC ACID | 325 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| ZESTORETIC | 12.5 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| LEVETIRACETAM | 750 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| BETAMETHASONE | 0.05 % | BID | Y-M: 20[redacted] | NOT REPORTED |
| CLOBETASOL | 0.05 % | PRN | Y-M: 20[redacted] | NOT REPORTED |
| OMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| PROMETHAZINE | 25 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| TRIAMCINOLONE | 0.5 % | BID | Y-M: 20[redacted] | NOT REPORTED |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] / -194 | NOT REPORTED |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -149 | NOT REPORTED |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -149 | Y-M: 20[redacted] / 226 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / 232 | ONGOING |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | RIGHT FALLOPIN TUBE CYST. |
| **Preferred term** | 卵管嚢胞 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 226 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 226): BILATERAL SALPHINGO-OOPHORECTOMY.: BENIGN BILATERAL OVARIES AND FALLOPIAN TUBE.; HYSTERECTOMY: BENIGN UTERUS; PATHOLOGY SPECIMEN OF RIGHT AND LEFT OVARIES: BENIGN BILATERAL OVARIES; PATHOLOGY SPECIMEN OF UTERUS: BENIGN UTERUS

| | |
|---|---|
| **AE Stopped Rx Day** | 226 |
| **Duration of AE** | 1 DAY |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | DYSMENORRHEA |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | RIGHT OVARY HEMORRHAGIC CYST. |
| **Preferred term** | 出血性卵巣嚢胞 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 226 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 226): SALPINGO-OOPHERECTOMY: SUBJECT RECOVERED

| | |
|---|---|
| **AE Stopped Rx Day** | 226 |
| **Duration of AE** | 1 DAY |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | DYSMENORRHEA |
| **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:** M15-572

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，右卵巣の出血性嚢胞及び右卵管嚢胞の事象を発現した。

**Event 1 及び 2 の臨床経過：**

関連する病歴は，局面型乾癬，高血圧，痙攣発作，脳卒中，乾癬性関節炎，現喫煙者（1 日 1 箱を 25 年間）及び元飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右卵巣の出血性嚢胞及び右卵管嚢胞を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右卵巣の出血性嚢胞及び右卵管嚢胞は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は複雑性嚢胞を伴う右卵巣腫瘤増大並びにきわめて重度の出血のため入院した。同日，被験者は子宮全摘術及び両側卵管卵巣摘出術を受けた。出血性黄体嚢胞のため，右卵巣のほうが大きかった。左卵巣には良性の出血性嚢胞が認められた。子宮には軽度の子宮頚管炎とともに，筋層内子宮筋腫及び限局性の不規則増殖内膜が認められた。悪性の徴候は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

**The patient's past medications include:**

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

Causality for UPADACITINIB (Blinded)

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1) Hemorrhagic ovarian cyst (10060783) (Haemorrhagic ovarian cyst (10060781) ) [v.23.0] [10060783]

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

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

**Dechallenge:** Not Applicable

2) Fallopian tube cyst (10050697) (Fallopian tube cyst (10050697) ) [v.23.0] [10050697]

**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)

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Event of RIGHT OVARY HEMORRHAGIC CYST

**- Investigator:** Dysmenorrhea

**- AbbVie:** Gynecologic cyst disease is common in the female population with prevalence of ovarian cysts between 8% and 18% in pre and post menopausal women and fallopian tube cysts representing approximately 10% of all adnexal masses in women 30's-40's years of age.

Event of RIGHT FALLOPIN TUBE CYST

**- Investigator:** Dysmenorrhea

**- AbbVie:** Gynecologic cyst disease is common in the female population with prevalence of ovarian cysts between 8% and 18% in pre and post menopausal women and fallopian tube cysts representing approximately 10% of all adnexal masses in women 30's-40's years of age.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] PATHOLOGY SPECIMEN OF RIGHT AND LEFT OVARIES:** benign bilateral ovaries

[redacted] **20[redacted] PATHOLOGY SPECIMEN OF UTERUS:** benign uterus

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 |
|---|---|---|---|---|
| 尿管結石症 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| ADA 40 mg EOW | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: TB VACCINE | 19[redacted] |
| DRUG ALLERGIES/REACTIONS: ALLERGY TO PENICILLIN | 19[redacted] |
| OTHER: PLAQUE PSORIASIS | 19[redacted] |
| HYPERTENSION | 20[redacted] |
| OTHER: VERTIGO | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: ELEVATED URIC ACID | 20[redacted] |
| CLOTTING/BLEEDING PROBLEMS: DEEP VEIN THOMBOSIS | 20[redacted] |
| DIABETES MELLITUS | 20[redacted] |
| OTHER: LATENT TB | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| Not reported. | |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 161 | 161 |
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 162 | [redacted]20[redacted] / 389 | 228 |
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 390 | | |

**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] |
| BCG Vaccine | NOT REPORTED | NOT REPORTED | Y-M: 19[redacted] |
| AMLODIPINE | 10 mg | QD | Y-M: 20[redacted] |
| APREMILAST | 30 mg | BID | Y-M: 20[redacted] |
| FEBUXOSTAT | 40 mg | QD | Y-M: 20[redacted] |
| VALSARTAN | 160/12.5 mg | QD | Y-M: 20[redacted] |
| GLIPIZIDE | 2.5 mg | BID | Y-M: 20[redacted] |
| MECLOZINE | 25 mg | PRN | Y-M: 20[redacted] |
| MELOXICAM | 15 mg | QD | Y-M: 20[redacted] / -280 |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -236 |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] / -236 |
| ISONIAZID | 300 mg | QD | Y-M: 20[redacted] / -18 |
| PYRIDOXINE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -18 |

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

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| AMLODIPINE | 10 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| FEBUXOSTAT | 40 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| VALSARTAN | 160/12.5 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| APREMILAST | 30 mg | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 390 |
| GLIPIZIDE | 2.5 mg | BID | Y-M: 20[redacted] | NOT REPORTED |
| MECLOZINE | 25 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| MELOXICAM | 15 mg | QD | Y-M: 20[redacted] / -280 | NOT REPORTED |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -236 | NOT REPORTED |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] / -236 | NOT REPORTED |
| PYRIDOXINE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -18 | NOT REPORTED |
| ISONIAZID | 300 mg | QD | Y-M: 20[redacted] / -18 | Y-M: 20[redacted] / 256 |
| KETOROLAC | 30 mg | OTHER: ONCE | Y-M: 20[redacted] / 64 | Y-M: 20[redacted] / 64 |
| MORPHINE | 4 mg | OTHER: ONCE | Y-M: 20[redacted] / 64 | Y-M: 20[redacted] / 64 |

**Event #1: Serious Adverse Event**

**Event Description** 3MM URETERAL CALCULUS

**Preferred term** 尿管結石症

**AE Onset Date / Rx Day** [redacted]20[redacted] / 64

**Age at AE Onset** 5[redacted]

**Laboratory Testing**

NOT REPORTED

**Microbiology**

[redacted]20[redacted] (RX DAY 65): URINE NPTST670-URINE CULTURE: Negative-GRAM NEGATIVE BACILLI, <10,000 CFU/ML

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 64): CT ABDOMEN AND PELVIS, WITHOUT CONTRAST: 3MM OBSTRUCTING STONE IN DISTAL URETER; [redacted]20[redacted] (RX DAY 65): CYSTOSCOPY, LEFT URETEROSCOPY, STONE EXTRACTION AND LEFT URETERAL STENT REPLACEMENT: STONE EXTRACTED AND STENT PLACED; XR UROGRAM RETROGRADE INTRAOP: FLUOROSCOPY FOR LEFT RETROGRADE UROGRAM AND STENT PLACEMENT

| | |
|---|---|
| **AE Stopped Rx Day** | 66 |
| **Duration of AE** | 3 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | HYPERCALCEMIA |
| **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:** M15-572

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，3 mm の尿管結石の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，高血圧，尿酸上昇，糖尿病，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 3 mm の尿管結石を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，3 mm の尿管結石は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，鼡径部に放射状に拡がる左側腹部痛のため救急治療室を受診した。腹部・骨盤 CT スキャン検査で 3 mm の左尿管結石が見つかった。Dilaudid の静脈内投与が開始された。左側腹部痛は鎮痛薬でコントロールすることができず，被験者はその後入院した。膀胱鏡検査時に結石除去が行われ，ステント留置が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，ketorolac，モルヒネ及び dilaudid であった。

**The patient's past medications include:**

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

PENICILLIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Ureteral calculus (10046383) (Ureterolithiasis (10077989) ) [v.22.1] [10046383]

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

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

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reactiondid not recur

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of 3MM URETERAL CALCULUS

**- Investigator:** HYPERCALCIUREA

**- AbbVie:** More likely related to underlying risk factors of elevated uric acid, diabetes and obesity.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] 20[redacted] **CT ABDOMEN AND PELVIS WITHOUT CONTRAST:** 3MM OBSTRUCTING STONE IN DISTAL URETER

[redacted] 20[redacted] **CYSTOSCOPY:** STONE EXTRACTED AND STENT PLACED

[redacted] 20[redacted] **LEFT URETEROSCOPY:** STONE EXTRACTED AND STENT PLACED

[redacted] 20[redacted] **URINE CULTURE:** Gram negative bacilli <10,000 CFU/ML

[redacted] 20[redacted] **X-RAY, UROGRAPHY RETROGRADE INTRAOP:** FLUOROSCOPY FOR LEFT RETROGRADE UROGRAM AND STENT PLACEMENT

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 |
|---|---|---|---|---|
| 呼吸窮迫 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 15 mg QD | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| DEPRESSION | 20[redacted] |
| HYPERTENSION | 20 |
| OSTEOARTHRITIS | 20 |
| GASTROESOPHAGEAL REFLUX DISEASE | 20 |
| OTHER: NARROW ESOPHAGUS | 20 |
| OTHER: CERVICAL SPONDYLOSIS | 20 |
| OTHER: LEFT SIDE MUXCLE WEAKNESS | 20 |
| TRANSIENT ISCHEMIC ATTACK: TIA | 20 |
| OTHER: SLEEP APNEA | 20 |
| OTHER: ARTHRALGIA RIGHT KNEE | 20 |
| DIABETES MELLITUS | 20 |
| OTHER: PLAQUE PSORIASIS | 20 |
| PSORIATIC ARTHRITIS | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: FRACTURED RIGHT ANKLE | 19 |
| SURGERY: L SPINE DISKECTOMY | 19 |
| SURGERY: C-SPINE FUSION | 20 |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 20 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 1 | [redacted] / 168 | 168 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 169 | [redacted] / 263 | 95 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ALPRAZOLAM | 1.0 mg | TID | Y-M: 20[redacted] |
| AMLODIPINE | 5.0 mg | QD | Y-M: 20[redacted] |
| PARACETAMOL | 325.00 mg | PRN | Y-M: 20[redacted] |
| PANTOPRAZOLE | 40.0 mg | QD | Y-M: 20[redacted] |
| ACETYLSALICYLIC ACID | 81.0 mg | QD | Y-M: 20[redacted] |
| METFORMIN | 250.00 mg | QD | Y-M: 20[redacted] |
| FOLIC ACID | 1.00 mg | QD | Y-M: 20[redacted] |
| METHOTREXATE | 20.00 mg | EVERY WEEK | Y-M: 20[redacted] |
| HYDROXYCHLOROQUINE | 200.00 mg | BID | Y-M: 20[redacted] / -292 |

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

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| ALPRAZOLAM | 1.0 mg | TID | Y-M: 20[redacted] | ONGOING |
| AMLODIPINE | 5.0 mg | QD | Y-M: 20[redacted] | ONGOING |
| PARACETAMOL | 325.00 mg | PRN | Y-M: 20[redacted] | ONGOING |
| PANTOPRAZOLE | 40.0 mg | QD | Y-M: 20[redacted] | ONGOING |
| ACETYLSALICYLIC ACID | 81.0 mg | QD | Y-M: 20[redacted] | ONGOING |
| FOLIC ACID | 1.00 mg | QD | Y-M: 20[redacted] | ONGOING |
| HYDROXYCHLOROQUINE | 200.00 mg | BID | Y-M: 20[redacted] / -292 | ONGOING |
| METHOTREXATE | 12.5 mg | EVERY WEEK | Y-M: 20[redacted] / 62 | ONGOING |
| GUAIFENESIN | 1 OTHER: TABLET | BID | Y-M: 20[redacted] / 143 | Y-M: 20[redacted] / 158 |
| MEDINITE | 2 OTHER: CAPSULES | QD | Y-M: 20[redacted] / 143 | Y-M: 20[redacted] / 158 |
| VICKS FORMULA 44M | 2 OTHER: CAPSULES | BID | Y-M: 20[redacted] / 143 | Y-M: 20[redacted] / 158 |
| AZITHROMYCIN | 500.00 mg | OTHER: ONCE | Y-M: 20[redacted] / 186 | Y-M: 20[redacted] / 186 |
| CEFTRIAXONE | 1000.00 mL | OTHER: ONCE | Y-M: 20[redacted] / 186 | Y-M: 20[redacted] / 186 |
| METHYLPREDNISOLONE | 125.00 mg | OTHER: ONCE | Y-M: 20[redacted] / 186 | Y-M: 20[redacted] / 186 |
| SALBUTAMOL | 3.00 mL | OTHER: ONCE | Y-M: 20[redacted] / 186 | Y-M: 20[redacted] / 187 |
| SODIUM CHLORIDE | 0.9 % | QD | Y-M: 20[redacted] / 186 | Y-M: 20[redacted] / 188 |
| FLUTICASONE | 250.00 OTHER: MCG | BID | Y-M: 20[redacted] / 188 | ONGOING |

| | | | | |
|---|---|---|---|---|
| SALBUTAMOL | 90.00 OTHER: MCG | QID | Y-M: 20[redacted] / 188 | ONGOING |
| TIOTROPIUM | 18.00 mg | QD | Y-M: 20[redacted] / 188 | ONGOING |
| AZITHROMYCIN | 250.00 mg | QD | Y-M: 20[redacted] / 188 | Y-M: 20[redacted] / 192 |
| PREDNISONE | 40.00 mg | QD | Y-M: 20[redacted] / 188 | Y-M: 20[redacted] / 202 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | UPPER RESPIRATORY DISTRESS |
| **Preferred term** | 呼吸窮迫 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 186 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 186): Glucose: 6.5 [3.9 - 5.5] MMOL/L; NPTST044-ANION GAP: 14 [3 - 11] UNSPECIFIED; NPTST481-O2SAT ART: 93.1 [96 - 97] %; NPTST521-PO2ART: 57.5 [80 - 100] MMHG; [redacted]20[redacted] (RX DAY 187): Glucose: 9.3 [3.9 - 5.5] MMOL/L; Leukocytes: 9.9 [4 - 11] 10^9/L; Lymphocytes/Leukocytes: 0.9 [1 - 1.4] %; NPTST044-ANION GAP: 17 [3 - 11] UNSPECIFIED; Neutrophils/Leukocytes: 80.6 [40 - 78] %

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 186): CHEST RADIOGRAPHS: NO ACUTE PULMONARY OR PLEURAL ABNORMALITY; ELECTROCARDIOGRAM: WITHIN NORMAL LIMITS

| | |
|---|---|
| **AE Stopped Rx Day** | 194 |
| **Duration of AE** | 9 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，上気道呼吸窮迫の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，元喫煙者（1 日 1 箱を 20 年間），高血圧，胃食道逆流性疾患，食道狭窄，頚椎融合，頚椎症，左側筋力低下，一過性脳虚血発作，睡眠時無呼吸，糖尿病，乾癬性関節炎

及び元飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は上気道呼吸窮迫を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，上気道呼吸窮迫は消失した。

本事象発現前，20[redacted] 年 [redacted] 月，被験者は上気道呼吸器感染（非重篤）を発現した。上気道呼吸器感染（非重篤）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸部うっ血及び喘鳴のため救急治療室を受診した。血液ガス分析では PO2 57.5 mmHg（室内気），O2 SAT 93.1%（室内気）と低かった。被験者は急性呼吸不全の診断で入院した。抗生物質の静脈内投与及びステロイドの経口投与による治療が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，スピリーバ，albuterol，メチルプレドニゾロン，塩化ナトリウム，アジスロマイシン，アルプラゾラム，フルチカゾン，prednisone 及びセフトリアキソンであった。

Causality for UPADACITINIB (Blinded)

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1) Respiratory distress (10038687) (Respiratory distress (10038687) ) [v.22.1] [10038687]

**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 UPPER RESPIRATORY DISTRESS

**- Investigator:** Not applicable

**- AbbVie:** event is more likely related to recent upper respiratory infection. Additional risk factors include significant past smoking history of 1 PPD for 20 years and pre-existing sleep apnea.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ANION GAP:** 14.0 Unspecified (normal 3.0 to 11.0)

[redacted] **20[redacted] ANION GAP:** 17.0 Unspecified (normal 3.0 to 11.0)

[redacted] **20[redacted] BLOOD PRESSURE:** 132/106mmHg

[redacted] **20[redacted] BODY TEMPERATURE:** 37 Degrees C

[redacted] **20[redacted] CHEST RADIOGRAPHS:** No acute pulmonary or pleural abnormality

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Within normal limits

[redacted] **20[redacted] GLUCOSE:** 117 mg/dL (normal 70.0 to 99.0)

[redacted] **20[redacted] GLUCOSE:** 167 mg/dL (normal 70.0 to 99.0)

[redacted] **20[redacted] HEART RATE:** 80 /min

[redacted] **20[redacted] LYMPHOCYTES %:** 0.9 % (normal 1.0 to 1.4)

[redacted] **20[redacted] NEUTROPHILS %:** 80.6 % (normal 40.0 to 78.0)

[redacted] **20[redacted] O2SAT ART:** 93.1 % (normal 96.0 to 97.0)

[redacted] **20[redacted] PO2ART:** 57.5 mmHg (normal 80 to 100)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9.9 10^3/uL (normal 4.0 to 11.0)

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 |
|---|---|---|---|---|
| 肺塞栓症 | X | X | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 15 mg QD | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: PLAQUE PSORIASIS | 19[redacted] |
| MIGRAINE HEADACHE | 19[redacted] |
| ASTHMA | 19[redacted] |
| PSORIATIC ARTHRITIS | 19[redacted] |
| OTHER: ANXIETY | 19[redacted] |
| OTHER: OCCASIONAL HEADACHE | 20[redacted] |
| OTHER: SEASONAL ALLERGIES | 20[redacted] |
| DEPRESSION | 20[redacted] |
| OBESITY | 20[redacted] |
| OTHER: VITAMIN D DEFICIENCY | 20[redacted] |
| OTHER: OSTEOARTHRITIC NODULES OF THE DISTAL IP JOINTS | 20[redacted] |
| OTHER: INSOMNIA | 20[redacted] |
| OSTEOARTHRITIS | 20[redacted] |
| OTHER: ITCHING | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: HYSTERECTOMY | 19[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0.5 PACK | 33 | 20[redacted] |
| CIGARS | FORMER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | FORMER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | 2 - 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 169 | 169 |

| | | | | | |
|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / [redacted]20[redacted] / 385 | 216 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 386[redacted]20[redacted] / 812 | 427 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| IBUPROFEN | 400 mg | TID | Y-M: 19[redacted] |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 19[redacted] |
| VACCINIUM MACROCARPON | 1 OTHER: TABLET | QD | Y-M: 19[redacted] |
| OCUVITE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] |
| UBIDECARENONE | 10 mg | QD | Y-M: 20[redacted] |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] |
| APREMILAST | 30 mg | BID | Y-M: 20[redacted] |
| CLOBETASOL | 1 OTHER: APPLICATION | BID | Y-M: 20[redacted] |
| OXYCODONE | 1 OTHER: TABLET | BID | Y-M: 20[redacted] / -329 |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] / -140 |
| ZOLPIDEM | 5 mg | QD | Y-M: 20[redacted] / -42 |
| DESONIDE | 1 OTHER: APPLICATION | BID | Y-M: 20[redacted] / -14 |
| VICODIN | 1 OTHER: TABLET | BID | Y-M: 20[redacted] / -14 |

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

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| IBUPROFEN | 400 mg | TID | Y-M: 19[redacted] | ONGOING |
| OCUVITE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] | ONGOING |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] | ONGOING |
| APREMILAST | 30 mg | BID | Y-M: 20[redacted] | ONGOING |
| VICODIN | 1 OTHER: TABLET | BID | Y-M: 20[redacted] / -14 | Y-M: 20[redacted] / 809 |
| DIPHENHYDRAMINE | 50 mg | BID | Y-M: 20[redacted] / 2 | ONGOING |
| RETINOL | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / 111 | ONGOING |
| DIPHENHYDRAMINE | 25 mg | QD | Y-M: 20[redacted] / 607 | ONGOING |
| MELATONIN | 3 mg | QD | Y-M: 20[redacted] / 795 | ONGOING |
| ALTEPLASE | 10 mg | OTHER: ONCE | Y-M: 20[redacted] / 808 | Y-M: 20[redacted] / 808 |
| ALTEPLASE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] / 808 | Y-M: 20[redacted] / 808 |
| SODIUM CHLORIDE | 25 mL | OTHER: HR | Y-M: 20[redacted] / 808 | Y-M: 20[redacted] / 808 |
| HEPARIN | 11 OTHER: UNITS/KG | OTHER: HR | Y-M: 20[redacted] / 808 | Y-M: 20[redacted] / 810 |
| SODIUM CHLORIDE | 2 mL | BID | Y-M: 20[redacted] / 808 | Y-M: 20[redacted] / 819 |
| POTASSIUM | 20 mEq | PRN | Y-M: 20[redacted] / 809 | Y-M: 20[redacted] / 811 |
| VICODIN | 2 OTHER: TABLETS | PRN | Y-M: 20[redacted] / 809 | Y-M: 20[redacted] / 818 |

| | | | | |
|---|---|---|---|---|
| PARACETAMOL | 650 mg | PRN | Y-M: 20[redacted] / 810 | Y-M: 20[redacted] / 818 |
| HEPARIN | 13 OTHER: UNITS/KG | OTHER: HR | Y-M: 20[redacted] / 811 | Y-M: 20[redacted] / 812 |
| HEPARIN | 3600 OTHER: UNITS | QD | Y-M: 20[redacted] / 811 | Y-M: 20[redacted] / 812 |
| WARFARIN | 5 mg | QD | Y-M: 20[redacted] / 811 | Y-M: 20[redacted] / 812 |
| HEPARIN | 15 OTHER: UNITS/KG | OTHER: HR | Y-M: 20[redacted] / 812 | Y-M: 20[redacted] / 812 |
| ENOXAPARIN | 90 mg | BID | Y-M: 20[redacted] / 812 | Y-M: 20[redacted] / 818 |
| WARFARIN | 6 mg | QD | Y-M: 20[redacted] / 813 | Y-M: 20[redacted] / 813 |
| RIOCIGUAT | 0.5 mg | TID | Y-M: 20[redacted] / 813 | Y-M: 20[redacted] / 819 |
| WARFARIN | 7.5 mg | QD | Y-M: 20[redacted] / 814 | Y-M: 20[redacted] / 816 |
| WARFARIN | 10 mg | QD | Y-M: 20[redacted] / 817 | Y-M: 20[redacted] / 818 |
| RIOCIGUAT | 9 mg | TID | Y-M: 20[redacted] / 819 | ONGOING |
| WARFARIN | 3 mg | QD | Y-M: 20[redacted] / 819 | Y-M: 20[redacted] / 827 |
| WARFARIN | 5 mg | QD | Y-M: 20[redacted] / 828 | ONGOING |

**Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Cardiovascular Events**

| | |
|---|---|
| **Event Description** | PULMONARY EMBOLISM |
| **Preferred term** | 肺塞栓症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 808 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 808): Basophils: 0 [0 - 0.3] 10^9/L; Basophils/Leukocytes: 0 [0 - 2] %; Calcium: 1.06 [1.15 - 1.29] MMOL/L; Chloride: 109 [98 - 107] MMOL/L; Eosinophils: 0 [0.1 - 0.5] 10^9/L; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 4 [4 - 5.2] 10^12/L; Glucose: 7.8 [3.9 - 5.5] MMOL/L; Hematocrit: 0.39 [0.36 - 0.47] FRACTION OF 1; Hemoglobin: 123 [120 - 155] G/L; Leukocytes: 13.6 [4.2 - 11] 10^9/L; Lymphocytes: 1.2 [1 - 4] 10^9/L; Lymphocytes/Leukocytes: 9 [20 - 44] %; Monocytes: 0.8 [0.3 - 0.9] 10^9/L; Monocytes/Leukocytes: 6 [2 - 9] %; NPTST122-BUN: 27 [6 - 20] MG/DL; NPTST179-CO2 TOTAL: 23 [19 - 24] MMOL/L; NPTST427-MCH: 30.6 [26 - 34] PG; NPTST428-MCHC: 31.4 [32 - 36.5] G/DL; NPTST429-MCV: 97.5 [78 - 100] FL; NPTST508-PERCENT IMMATUREGRANULACTYES: 1 [NOT REPORTED - NOT REPORTED] %; NPTST563-RDW-CV: 12.7 [11 - 15] %; NPTST644-TROPONIN: 0.81 [NOT REPORTED - 0.1] ng/mL; NPTST646-TROPONIN I: 1.00 [NOT REPORTED - 0.05] ng/mL; NPTST646-TROPONIN I: 1.10 [NOT REPORTED - 0.05] ng/mL; Neutrophils: 11.5 [1.8 - 7.7] 10^9/L; Neutrophils/Leukocytes: 84 [50 - 70] %; Platelets: 115 [140 - 450] 10^9/L; Potassium: 4 [3.4 - 5.1] MMOL/L; Sodium: 141 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 819): Erythrocytes: 3.3 [4 - 5.2] 10^12/L; Hematocrit: 0.32 [0.36 - 0.47] FRACTION OF 1; Hemoglobin: 100 [120 - 155] G/L; Leukocytes: 6.6 [4.2 - 11] 10^9/L; NPTST427-MCH: 30.5 [26 - 34] PG; NPTST428-MCHC: 31.2 [32 - 36.5] G/DL; NPTST429-MCV: 97.9 [78 - 100] FL; NPTST473-NRBC: 0 [0 - 100] 099,WBC; NPTST563-RDW-CV: 13.7 [11 - 15] %; Platelets: 298 [140 - 450] 10^9/L

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 808): CHEST CT: POSITIVE FOR PE, LARGE CLOT BURDEN. NEGATIVE FOR INFECTION. SEVERAL PULMONARY NODULES INCLUDING SUB 3 MM PULMONARY NODULES.; CHEST X-RAY: NO ACUTE PULMONARY PROCESS; ELECTROCARDIOGRAM: RATE: 125, RHYTHM: SINUS TACHYCARDIA,

ABNORMALITY: RSR' OR QR PATTERN IN V1 SUGGESTS RIGHT VENTRICULAR CONDUCTION DELAY. MARKED ST ABNORMALITY, POSSIBLE INFERIOR SUBENDOCARDIAL INJURY. COMPARED WITH PRIOR EKG: ST DEPRESSION IN INFERIOR AND LATERAL LEADS; LOWER EXTREMITY ULTRASOUND: ECHOGENIC MATERIAL WITHIN THE VISUALIZED PORTION OF THE LEFT COMMON FEMORAL VEIN, LIKELY PARTIALLY OCLUSIVE THROMBUS. SHORT INTERVAL FOLLOW UP ULTRASOUND COULD BE CONSIDERED. NO ULTRASOUUND EVIDNECEOF DEEP VENOUS THROMBOSIS IN THE RIGHT LOWER EXTREMITY.; [redacted]20[redacted] (RX DAY 809): ECHOCARDIOGRAM: SEVERE RV SYSTOLIC DYSFUNCTION. MILD PULMONARY HYPERTENTION.; [redacted]20[redacted] (RX DAY 810): ECHOCARDIOGRAM: MILDLY INCREASED RV SIZE WITH MILDLY DECREASED SYSTOLIC FUNCTION. MODERATE PULMONARY HYPERTENTION. PASP 67,. COMPARED TO PREVIOUS STUDY, RV SIZE DECREASED ND FUNCTION IMPROVED.; [redacted]20[redacted] (RX DAY 812): LIMITED ECHOCARDIOGRAM: MODRATE PULMONARY HYPERTENSION, PASP=53 MMHG. MIDLY INCREASED RV SIZE WITH MILDLY DECREASED SYSTOLIC FUNCTION. AGITATED SALINE WAS INGECTED THROUGH A PERIPHERAL VEIN AND DID NOT SHOW EVIDENCE OF A SHUNT.

| | |
|---|---|
| **AE Stopped Rx Day** | 819 (7 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 12 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION, LIFE THREATENING |

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

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，肺塞栓症の事象を発現した。

**Event 2 の臨床経過：**

関連する病歴は，局面型乾癬，片頭痛，乾癬性関節炎，元喫煙者（1 日 0.5 箱を 33 年間），肥満，変形性関節症，元喫煙者（パイプ及び葉巻），元飲酒者（1 日 2～4 杯），深部静脈血栓症の家族歴，血沈亢進及び麻薬性鎮痛薬の長期使用であった。深部静脈血栓症の家族歴もあった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺塞栓症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肺塞栓症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右側胸痛及び息切れで救急科を受診した。胸痛は両肩に放射状に拡がった。被験者は過去にも同様の疼痛及び息切れを経験していたが，今回は「死んでしま

うのではないか」と感じられるほどのものであった。また，その日の朝，被験者は気絶して転倒した。被験者は右下肢痛及び左下肢腫脹（非重篤な深部静脈血栓症と診断された）も呈していた。被験者は低血圧の状態にあり，収縮期血圧が 80 台であった。またトロポニン増加及び BNP 値増加が認められた。被験者は CT 検査を受け，肺に大きな血栓が認められた。被験者は tPA を投与され，ICU に入室した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者は抗凝固薬を使用しておらず，遠距離の旅行歴，入院歴及び手術歴もなかった。深部静脈血栓症や肺塞栓症の病歴もなかった。喫煙歴があったが，禁煙していた。

治験責任医師は，肥満及び体を動かすことの少ない生活であることが本事象の危険因子であったと述べた。被験者には深部静脈血栓症の強力な家族歴があり，父親と 2 人の兄弟が長期にわたって抗凝固療法を受けていた。

本事象により治験薬の投与は中止された。

投与された薬剤は，塩化カリウム，ワルファリン，酸素，ヘパリン，asa，tpa，塩化ナトリウム，porcine-fastact，coumadin，lovenox，activase 及びタイレノールであった。

**The patient's past medications include:**

METHOTREXATE for PSORIATIC ARTHRITIS (19[redacted] - 19[redacted])

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

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

MEDROL DOSEPACK for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for UPADACITINIB (Blinded)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377) ) [v.23.0] [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

Alternative Etiology for UPADACITINIB (Blinded)

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Event of PULMONARY EMBOLISM

**- Investigator:** Not applicable

**- AbbVie:** More likely related to risk factors such as strong family history of DVT (including father and siblings), obesity, pre-existing psoriasis, and age. Patients older than 40 years old are at higher risk of VTE and that risk doubles with each subsequent decade.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] A/G RATIO:** 0.9 no units

[redacted] **20[redacted] ALBUMIN:** 3.6 no units

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 58 no units

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 52 no units

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 44 no units

[redacted] **20[redacted] ANION GAP:** 14 no units

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 34 no units

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 34 no units

[redacted] **20[redacted] BILIRUBIN:** 0.5 no units

[redacted] **20[redacted] BLOOD PRESSURE:** Hypotensive in the ED with SBP 80's mmHg.

[redacted] **20[redacted] BLOOD PRESSURE:** 103/66 mmHg

[redacted] **20[redacted] BMI:** 33.4 No units

[redacted] **20[redacted] BUN:** 27 mg/dL (normal 6 to 20)

[redacted] **20[redacted] BUN:** 16 mg/dL

[redacted] **20[redacted] CALCIUM IONIZED:** 1.21 no units

[redacted] **20[redacted] CALCIUM:** 1.06 MMOL/L (normal 1.15 to 1.29)

[redacted] 20[redacted] **CHEST X-RAY:** No acute cardiopulmonary process. Cardiac silhouette and pulmonary vasculature are within normal limits. No pneumothorax, pleural effusion, or focal airspace opacity. No acute bony abnormality. Minimal right hemidiaphragm elevation. Old left rib deformity.

[redacted] 20[redacted] **CHLORIDE:** 109 MMOL/L (normal 98 to 107)

[redacted] 20[redacted] **CO2:** 23 MMOL/L (normal 19 to 24)

[redacted] 20[redacted] **CO2:** 27 MMOL/L

[redacted] 20[redacted] **CREATININE:** 0.90 no units

[redacted] 20[redacted] **CREATININE:** 0.88 no units

[redacted] 20[redacted] **CT ANGIOGRAM CHEST:** Chest: Good opacification of pulmonary arteries. PE Summary: Most proximal PE right: Proximal right pulmonary artery. Most proximal PE left: Proximal left pulmonary artery. Subjective Bilateral PE Burden: Large. Septal Flattening/Bowing: Yes. RV/LV Ratio:1.4. Coronary artery sclerosis. Heart size is not enlarged. No pericardial effusion. Thoracic aorta is grossly unremarkable besides mild atherosclerosis. No suspicious adenopathy. Visualized thyroid gland demonstrates no focal abnormalities. Probably reactive mildly prominent left supraclavicular nodes. Small sliding hiatal hernia. No suspicious intrathoracic adenopathy. Limited evaluation of the upper abdomen. Reflux of contrast into the hepatic veins. probably partial visualization of left renal cyst. Probably nodular lingular atelectasis. Several sub-3mm pulmonary nodules. For example, 0.2 cm left apical nodule and 0.2 cm right midlung nodule.

[redacted] 20[redacted] **CT SCAN:** Positive for PE: large clot burden from main pulmonary arteries into the distal segments with associated right heart strain. Negative for infection within the chest. Several sub +3mm pulmonary nodules. Recommend follow-up per Fleischner Society criteria guidelines.

[redacted] 20[redacted] **ECHOCARDIOGRAM:** Bilateral Pulmonary embolism s/p tPA ([redacted] 20[redacted]). Moderate RV cavity enlargement. Severe RV systolic dysfunction McConnell's sign. Septal flattening consistent with RV volume overload. Mild pulmonary hypertension, RSVP 39 mmHg. Normal LV size and systolic function, LVEF 65%. No significant valvular abnormalities. Small pericardial effusion.

[redacted] 20[redacted] **ECHOCARDIOGRAM:** S/P TPA for Pulmonary embolism: mildly increased right ventricular size with mildly decreased systolic function. Moderate Pulmonary hypertension with RPASP 67 mmHg. Compared to prior echo dated [redacted] 20[redacted], RV size has significantly decreased and function has improved.

[redacted] 20[redacted] **ECHOCARDIOGRAM:** MODERATE PULMONARY, PASP=53 MMhG. MILD INCREASED RV SIZE WITH MILDLY DECREASED SYSTOLIC FUNCTION. AGITATED SALINE WAS INJECTED THROUGH A PERIPHERAL VEIN AND DID NOT SHOW¥ EVIDENCE OF A SHUNT.

[redacted] 20[redacted] **EGFR AFRICAN AMERICAN:** 77 mL/min/1.73m2

[redacted] 20[redacted] **EGFR NON AFRICAN AMERICAN:** 67 mL/min/1.73m2

[redacted] 20[redacted] **EKG:** Rate 125, rhythm sinus tachycardia. RSR or QR pattern in V1 suggests right ventricular conduction delay. Marked ST abnormality, possible inferior subendocardial injury. Compared with prior EKG (date unknown): ST depression in inferior and lateral leads.

[redacted] 20[redacted] **GLOBULIN:** 3.9 no units

[redacted] **20[redacted] GLUCOSE:** 141 mg/dL (normal 70 to 99)

[redacted] **20[redacted] GLUCOSE:** 93 mg/dL

[redacted] **20[redacted] GPT:** 42 no units

[redacted] **20[redacted] HEMATOCRIT:** 39.1 % (normal 36.0 to 46.5)

[redacted] **20[redacted] HEMATOCRIT:** 30.4 %

[redacted] **20[redacted] HEMOGLOBIN:** 12.3 G/DL (normal 12.0 to 15.5)

[redacted] **20[redacted] INR:** 1.1 no units

[redacted] **20[redacted] IONIZED CALCIUM:** 1.06 no units

[redacted] **20[redacted] LIPASE:** 90 no units

[redacted] **20[redacted] LYMPHOCYTES:** 6 no units

[redacted] **20[redacted] MAGNESIUM:** 2.2 no units

[redacted] **20[redacted] NEUTROPHIL:** 89 no units

[redacted] **20[redacted] OXYGEN SATURATION:** 98 %

[redacted] **20[redacted] OXYGEN SATURATION:** 88 %

[redacted] **20[redacted] PLATELET COUNT:** 103 no units

[redacted] **20[redacted] PLATELET COUNT:** 126 no units

[redacted] **20[redacted] POTASSIUM:** 4.0 MMOL/L (normal 3.4 to 5.1)

[redacted] **20[redacted] PRO-BNP:** 1775 No units

[redacted] **20[redacted] PARTIAL PROTHROMBIN TIME:** 43 no units

[redacted] **20[redacted] PULSE:** 126 /min

[redacted] **20[redacted] PULSE:** 133 /min

[redacted] **20[redacted] RBC:** 4.02 mil/mcl (normal 4.00 to 5.20)

[redacted] **20[redacted] RESPIRATORY RATE:** 18 /min

[redacted] **20[redacted] SODIUM:** 141 no units

[redacted] **20[redacted] SODIUM:** 139 no units

[redacted] **20[redacted] BODY TEMPERATURE:** 97.6 F

[redacted] **20[redacted] TOTAL BILIRUBIN:** 0.3 no units

[redacted] **20[redacted] TOTAL PROTEIN:** 7.5 no units

[redacted] **20[redacted] TROPONIN:** 0.81 NG/ML (normal <0.10)

[redacted] **20[redacted] TROPONIN I:** 1.10 NG/ML (normal <0.05)

[redacted] **20[redacted] ULTRASOUND:** Echogenic material within the visualized portion of the left common femoral vein, likely partially occlusive thrombus. Short interval follow-up ultrasound could be considered. No ultrasound evidence of deep vein thrombosis in the right lower extremity. Left popliteal cyst.

[redacted] **20[redacted] WBC:** 13.6 k/mcl (normal 4.2 to 11.0)

[redacted] **20[redacted] WBC:** 5.7 k/mcl

[redacted] **20[redacted] WBC:** 6.6 k/mcl

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 |
|---|---|---|---|---|
| 骨壊死 | X | | | |

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

| Medical History | Onset Year |
|---|---|
| OTHER: PANIC DISORDER | 19[redacted] |
| OTHER: SEASONAL ALLERGIES | 20[redacted] |
| DEPRESSION | 20[redacted] |
| OTHER: ANXIETY | 20[redacted] |
| DIABETES MELLITUS | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| OTHER: TACHYCARDIA | 20[redacted] |
| HYPOTHYROIDISM | 20[redacted] |
| OTHER: L PROXIMAL HUMERUS FRACTURE | 20[redacted] |
| OTHER: TROUBLE SLEEPING | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: HAIR LOSS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: PARTIAL HYSTERECTOMY | 19[redacted] |
| SURGERY: SURGICAL REPAIR OF L SHOULDER FRACTURE | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | CURRENT | 0.25 PACK | 1 | |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

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

| | | | | | | |
|---|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 170 | [redacted]20[redacted] / 392 | 223 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 393 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| FLUOXETINE | 40 mg | QD | Y-M: 20[redacted] |
| SALBUTAMOL | 1 OTHER: PUFF | PRN | Y-M: 20[redacted] |
| METFORMIN | 1000 mg | QD | Y-M: 20[redacted] |
| METOPROLOL | 75 mg | QD | Y-M: 20[redacted] |
| SERETIDE | 1 OTHER: PUFF | PRN | Y-M: 20[redacted] |
| LEVOTHYROXINE | 100 ug | QD | Y-M: 20[redacted] |
| SITAGLIPTIN | 100 mg | QD | Y-M: 20[redacted] |
| TRAZODONE | 50 mg | PRN | Y-M: 20[redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] |
| FOLIC ACID | 2 mg | QD | Y-M: 20[redacted] / -259 |
| ALPRAZOLAM | 0.25-0.5 mg | PRN | Y-M: 20[redacted] / -247 |
| BUSPIRONE | 10 mg | QD | Y-M: 20[redacted] / -247 |
| FOLIC ACID | 5 mg | QD | Y-M: 20[redacted] / -222 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -222 |
| HERPES ZOSTER IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] / -199 |

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

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| FLUOXETINE | 40 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| SALBUTAMOL | 1 OTHER: PUFF | PRN | Y-M: 20[redacted] | NOT REPORTED |
| METFORMIN | 1000 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| METOPROLOL | 75 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| SERETIDE | 1 OTHER: PUFF | PRN | Y-M: 20[redacted] | NOT REPORTED |
| LEVOTHYROXINE | 100 ug | QD | Y-M: 20[redacted] | NOT REPORTED |
| SITAGLIPTIN | 100 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| TRAZODONE | 50 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| ALPRAZOLAM | 0.25-0.5 mg | PRN | Y-M: 20[redacted] / -247 | NOT REPORTED |
| BUSPIRONE | 10 mg | QD | Y-M: 20[redacted] / -247 | NOT REPORTED |

| | | | | |
|---|---|---|---|---|
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -222 | NOT REPORTED |
| FOLINIC ACID | 10 mg | EVERY WEEK | Y-M: 20[redacted] / 31 | NOT REPORTED |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] / 275 | Y-M: 20[redacted] / 298 |
| METHYLPREDNISOLONE | 2 mg | QD | Y-M: 20[redacted] / 299 | Y-M: 20[redacted] / 302 |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] / 303 | Y-M: 20[redacted] / 310 |
| METHYLPREDNISOLONE | 2 mg | QD | Y-M: 20[redacted] / 311 | Y-M: 20[redacted] / 368 |
| NITROFURANTOIN | 100 mg | BID | Y-M: 20[redacted] / 316 | Y-M: 20[redacted] / 321 |
| PARACETAMOL | 650 mg | PRN | Y-M: 20[redacted] / 316 | Y-M: 20[redacted] / 379 |
| TRAMADOL | 50 mg | OTHER: EVERY 6 HRS AS NEEDED | Y-M: 20[redacted] / 369 | ONGOING |
| CEFAZOLIN | UNKNOWN OTHER: UNKNOWN DOSE | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| CHLORHEXIDINE | 1 OTHER: APPLICATION | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| CLONIDINE | 25 ug | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| DEXAMETHASONE | 8 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| EPHEDRINE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| FENTANYL | 25 ug | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| FLEBOBAG RING LACT | 800 mL | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| GLYCOPYRRONIUM | 0.6 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| LIDOCAINE | 3 OTHER: UNKNOWN | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| METOPROLOL | 5 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| MIDAZOLAM | 1 mg | OTHER: EVERY 5 MIN AS NEEDED | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| NEOSTIGMINE | 3 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| ONDANSETRON | 4 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| PHENYLEPHRINE | 3800 ug | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| PROCHLORPERAZINE | 5 mg | OTHER: EVERY 30 MIN AS NEEDED | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| PROMETHAZINE | 12.5 mg | OTHER: EVERY 30 MIN AS NEEDED | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |
| PROPOFOL | 234.17 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 | Y-M: 20[redacted] / 369 |

| | | | |
|---|---|---|---|
| PROPOFOL | 350 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369 |
| ROCURONIUM | 50 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369 |
| ROPIVACAINE | 25 mL | OTHER: ONCE | Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369 |
| SODIUM CHLORIDE | 112.8 mL | OTHER: ONCE | Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369 |
| TRANEXAMIC ACID | 1280 mg | OTHER: ONCE | Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369 |
| BACITRACIN | 50,000 OTHER: UNITS | OTHER: ONCE | Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 370 |
| VANCOMYCIN | 1 g | BID | Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 370 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | COLLAPSED AVASCULAR NECROSIS OF THE LEFT HUMERAL HEAD WITHOUT OBVIOUS GLENOID INVOLVEMENT. |
| **Preferred term** | 骨壊死 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 313 |
| **Age at AE Onset** | 7[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 369): Glucose: 6.8 [3.6 - 11] MMOL/L

**Microbiology**

[redacted]20[redacted] (RX DAY 369): OTHER JOINT FLUID NPTST117-BODY FLUID CULTURE, AEROBIC AND: Negative

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 369): HEMIARTHROPLASTY OF LEFT SHOULDER, REMOVAL OF OLD FIXATION HARDWARE: INTERVAL EXPLANT OF FIXATION HARDWARE AND PLACEMENT OF LEFT SHOULDER RESURFACING ARTHROPLASTY; OXYGEN: USED DURING SURGERY: CONTINUOUS,TITRATE O2 TO KEEP SPO2 GREATER THAN 92%; X-RAY OF LEFT SHOULDER: INTERVAL PLACEMENT OF A RESURFACING LEFT SHOULDER ARTHROPLASTY, NO DISLOCATION, THERE IS NO LOOSENING OR FRACTURE; [redacted]20[redacted] (RX DAY 370): PHYSICAL THERAPY SESSIONS: POST OP PLAN WILL BE THE STANDARD SHOULDER ARTHROPLASTY PHYSICAL THERAPY PROTOCOL BEGINNING ON POST OP DAY 1. PATIENT WILL BEGIN WTIH 30 DEGRESS PASSIVE SUPINE EXTERNAL ROTATION AT THE SIDE AND 130 DEGREES PASSIVE SUPINE FORWARD ELEVATION.

| | |
|---|---|
| **AE Stopped Rx Day** | 369 |
| **Duration of AE** | 57 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | HEMIARTHROPLASTY OF L SHOULDER |
| **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:** M15-572

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，圧迫による上腕骨頭無腐性壊死（明らかな関節窩への拡がりなし）の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，糖尿病，甲状腺機能低下症，左近位上腕骨骨折，左肩骨折の外科的修復，乾癬性関節炎，現喫煙者（1 日 0.25 箱を 1 年間）及び元飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は圧迫による上腕骨頭無腐性壊死（明らかな関節窩への拡がりなし）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，圧迫による上腕骨頭無腐性壊死（明らかな関節窩への拡がりなし）は消失した。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，持続する痛みと左肩関節機能障害に対する半関節形成術のため入院した。被験者は，近位上腕骨骨折に対する観血的整復と内固定を受けた後であった。術後経過は良好で，痛みはコントロールすることができた。術後 1 日目，経口鎮痛薬に切り替えられ，十分な効果が認められた。被験者は運動及びモビライゼーションのために理学療法を開始した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，リドカイン，セファゾリン，アセトアミノフェン，アスピリン 81，ヒドロモルフォン，ポリエチレングリコール，senna docusate，メドロール，バンコマイシン，トラマドール，プロクロルペラジン，プロメタジン，バシトラシン，lactated ringers，クロルヘキシジン，フェンタニル，エフェドリン，塩化ナトリウム，フェニレフリン，トラネキサム酸，glycopyrrolate，ネオスチグミン，デキサメタゾン，ミダゾラム，ロクロニウム，プロポフォール，ロピバカイン，クロニジン，メドロール及びオンダンセトロンであった。

Causality for UPADACITINIB (Blinded)

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1) Aseptic necrosis of head of humerus (10003464) (Osteonecrosis (10031264) ) [v.22.1] [10003464]

**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 COLLAPSED AVASCULAR NECROSIS OF THE HUMERAL HEAD WITHOUT OBVIOUS GLENOID INVOLVEMENT

**- Investigator:** Hemiarthroplasty of left shoulder

**- AbbVie:** Risk factors include pre-existing history of L. proximal humerus fracture and subsequent open reduction internal fixation, and chronic concomitant therapy with methylprednisolone.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] BODY FLUID CULTURE, AEROBIC AND ANAEROBIC:** Negative

[redacted] **20[redacted] GLUCOSE:** 122 mg/dL

[redacted] **20[redacted] X-RAY OF LEFT SHOULDER:** Interval placement of resurfacing left shoulder arthroplasty, no dislocation. There is no loosening or fracture

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 | | | |
| 脊柱管狭窄症 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 30 mg QD | 7[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| DEPRESSION | 19[redacted] |
| NEPHROLITHIASIS | 19[redacted] |
| OTHER: ANXIETY | 19[redacted] |
| MIGRAINE HEADACHE | 19[redacted] |
| OTHER: SWEATING EPISODES | 19[redacted] |
| OTHER: PRE-DIABETES | 20[redacted] |
| GASTROESOPHAGEAL REFLUX DISEASE: DUE TO HIATAL HERNIA | 20[redacted] |
| OTHER: HIATAL HERNIA | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| OTHER: LICHEN SCLEROSIS | 20[redacted] |
| OTHER: BILATERAL CARPAL TUNNEL SYNDROME | 20[redacted] |
| OTHER: INSOMNIA | 20[redacted] |
| OTHER: SLEEP APNEA | 20[redacted] |
| OSTEOARTHRITIS | 20[redacted] |
| OTHER: ELEVATED CK | 20[redacted] |
| OTHER: REACTIVE AIRWAY | 20[redacted] |
| OTHER: TRIGGER FINGER RELEASE, BILATERAL 3RD FINGER | 20[redacted] |
| OTHER: DRY EYES | 20[redacted] |
| OTHER: CONSTIPATION | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: SPINAL STENOSIS | 20[redacted] |
| HYPERLIPIDEMIA: ELEVATED CHOLESTEROL LEVELS | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| OTHER: SEASONAL ALLERGIES | 20[redacted] |
| OTHER: STRESS INCONTINENCE | 20[redacted] |
| OTHER: BAKER'S CYST R KNEE | 20[redacted] |
| OTHER: URINARY TRACT INFECTION | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| INCREASED CREATINE PHOSPHOKINASE: HOLDING IMP AND REPEAT LAB IN 2 WEEKS | NOT REPORTED |
| INCREASED CREATINE PHOSPHOKINASE: REPEAT CK | NOT REPORTED |
| SURGERY: L4-L5 FUSION | 19[redacted] |

| | |
|---|---|
| SURGERY: BILATERAL CORN AND BUNIONECTOMY | 20[redacted] |
| SURGERY: R HIP REPLACEMENT | 20[redacted] |
| SURGERY: BLADDER SLING PLACEMENT | 20[redacted] |
| SURGERY: L KNEE REPLACEMENT | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 2 PACK | 4 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 168 | 168 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 169 | [redacted]20[redacted] / 386 | 218 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 387 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ESCITALOPRAM | 20 mg | QD | Y-M: 20[redacted] |
| HERPES ZOSTER IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MELATONIN | 5 mg | QD | Y-M: 20[redacted] |
| RANITIDINE | 150 mg | QD | Y-M: 20[redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] |
| CALCIUM | 1 OTHER: PACKET | QD | Y-M: 20[redacted] |
| LOSARTAN | 50 mg | QD | Y-M: 20[redacted] |
| MONTELUKAST | 10 mg | QD | Y-M: 20[redacted] |
| PRAVASTATIN | 10 mg | QD | Y-M: 20[redacted] |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] |
| BUPROPION | 300 mg | QD | Y-M: 20[redacted] |
| AMOXICILLIN | 2000 mg | PRN | Y-M: 20[redacted] |
| TRAMADOL | 50 mg | PRN | Y-M: 20[redacted] |
| FLUTICASONE | 1 OTHER: SPRAY | PRN | Y-M: 20[redacted] |
| GABAPENTIN | 600 mg | QD | Y-M: 20[redacted] |
| IPRATROPIUM | 0.03 % | PRN | Y-M: 20[redacted] |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted] / -45 |

**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 |
|---|---|---|---|---|
| ESCITALOPRAM | 20 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| MELATONIN | 5 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| RANITIDINE | 150 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 253 |
| LOSARTAN | 50 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| MONTELUKAST | 10 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| PRAVASTATIN | 10 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| CALCIUM | 1 OTHER: PACKET | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 444 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] | Y-M: 20[redacted] / 169 |
| BUPROPION | 300 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| AMOXICILLIN | 2000 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| TRAMADOL | 50 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| FLUTICASONE | 1 OTHER: SPRAY | PRN | Y-M: 20[redacted] | NOT REPORTED |
| GABAPENTIN | 600 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| IPRATROPIUM | 0.03 % | PRN | Y-M: 20[redacted] | NOT REPORTED |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted] / -45 | NOT REPORTED |
| VACCINIUM MACROCARPON | 500 mg | QD | Y-M: 20[redacted] / 16 | NOT REPORTED |
| ESTRADIOL | 2 g | OTHER: TWICE PER WEEK | Y-M: 20[redacted] / 22 | NOT REPORTED |
| PROPRANOLOL | 10 mg | PRN | Y-M: 20[redacted] / 44 | NOT REPORTED |
| DIPHENHYDRAMINE | 50 mg | PRN | Y-M: 20[redacted] / 58 | NOT REPORTED |
| CHLORHEXIDINE | 15 mL | BID | Y-M: 20[redacted] / 81 | Y-M: 20[redacted] / 87 |
| HYDROCORTISONE | 1 OTHER: LIGHT APPLICATION | BID | Y-M: 20[redacted] / 122 | Y-M: 20[redacted] / 129 |
| LIDOCAINE | 5 % | QD | Y-M: 20[redacted] / 155 | Y-M: 20[redacted] / 185 |
| LOTRISONE | 1 OTHER: APPLICATION | BID | Y-M: 20[redacted] / 169 | Y-M: 20[redacted] / 235 |

| | | | | |
|---|---|---|---|---|
| OXYCODONE | 5 mg | BID | Y-M: 20[redacted]/ 187 | Y-M: 20[redacted]/ 208 |
| PARACETAMOL | 500-1000 mg | OTHER: EVERY 4-6 HRS PRN | Y-M: 20[redacted]/ 187 | Y-M: 20[redacted]/ 208 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted]/ 199 | Y-M: 20[redacted]/ 305 |
| PARACETAMOL | 1000 mg | QD | Y-M: 20[redacted]/ 209 | NOT REPORTED |
| FOLIC ACID | 3 mg | QD | Y-M: 20[redacted]/ 254 | NOT REPORTED |
| IBUPROFEN | 600 mg | TID | Y-M: 20[redacted]/ 254 | NOT REPORTED |
| LEVOFLOXACIN | 250 mg | QD | Y-M: 20[redacted]/ 284 | Y-M: 20[redacted]/ 294 |
| METHENAMINE | 1000 mg | QID | Y-M: 20[redacted]/ 302 | ONGOING |
| METRONIDAZOLE | 1 OTHER: APPLICATION | BID | Y-M: 20[redacted]/ 309 | NOT REPORTED |
| METHOTREXATE | 10 mg | EVERY WEEK | Y-M: 20[redacted]/ 312 | NOT REPORTED |
| KETOROLAC | 10 mg | QID | Y-M: 20[redacted]/ 320 | Y-M: 20[redacted]/ 320 |
| KETOROLAC | 30 mg | OTHER: ONCE | Y-M: 20[redacted]/ 320 | Y-M: 20[redacted]/ 320 |
| ONDANSETRON | 4 mg | OTHER: ONCE | Y-M: 20[redacted]/ 320 | Y-M: 20[redacted]/ 320 |
| SODIUM CHLORIDE | 1000 mL | OTHER: ONCE | Y-M: 20[redacted]/ 320 | Y-M: 20[redacted]/ 320 |
| TAMSULOSIN | 0.4 mg | QD | Y-M: 20[redacted]/ 320 | Y-M: 20[redacted]/ 327 |
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted]/ 320 | Y-M: 20[redacted]/ 332 |
| VICODIN | 5/325 mg | PRN | Y-M: 20[redacted]/ 320 | Y-M: 20[redacted]/ 333 |
| ATROPINE | 0.5 mg | OTHER: ONCE | Y-M: 20[redacted]/ 321 | Y-M: 20[redacted]/ 322 |
| CEFTRIAXONE | 1 g | OTHER: ONCE | Y-M: 20[redacted]/ 321 | Y-M: 20[redacted]/ 322 |
| FLEBOBAG RING LACT | 1000 mL | OTHER: ONCE | Y-M: 20[redacted]/ 321 | Y-M: 20[redacted]/ 322 |
| HYDROCORTISONE | 100 mg | OTHER: ONCE | Y-M: 20[redacted]/ 321 | Y-M: 20[redacted]/ 322 |
| MIDAZOLAM | 2 mg | OTHER: ONCE | Y-M: 20[redacted]/ 321 | Y-M: 20[redacted]/ 322 |
| ONDANSETRON | 8 mg | OTHER: ONCE | Y-M: 20[redacted]/ 321 | Y-M: 20[redacted]/ 322 |
| AMOXICILLIN | 500 mg | TID | Y-M: 20[redacted]/ 325 | Y-M: 20[redacted]/ 327 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING OF PRE-EXISTING SPINAL STENOSIS |
| **Preferred term** | 脊柱管狭窄症 |

| | |
|---|---|
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 107 |
| **Age at AE Onset** | 7[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 114): MRI OF LUMBAR SPINE: NO ACUTE FRACTURE OR SUBLUXATION. THAT IS POST LUMBAR FUSION FROM L4 THROUGH S1 WITH LAMINECTOMY CHANGES AT L4 AND L5. WHEN COMPARED TO THE PREVIOUS EXAMINATION, DISC DISEASE FROM L1-L2 THROUGH L5-S1REMAIN STABLE. THERE IS A SLIGHT PROGRESSION OF DISC DISEASE AT T9-T10, T10-T11 AND T11-T12. CENTRAL STENOSIS AT L3-L4 BEING STABLE. FORAMINAL ENCROACHMENT WITH IMPINGEMENT OF THE EXITING RIGHT L3 TO AND L3 NERVE ROOTS REMAIN UNCHANGED.; [redacted]20[redacted] (RX DAY 187): LAMINECTOMY: STABLE STATUS POST LUMBAR LAMINECTOMY L1-L4 WITH EXCISION SYNOVIAL CYST AT L3-4.; XR OF LUMBAR SPINE: INTRAOPERATIVE VIEW DEMONSTRATING REMOTE POSTERIOR FUSION FROM L3 THROUGH S1. SURGICAL RETRACTOR IS IN PLACE POSTERIORLY. THERE ARE 2 METALLIC SURGICAL PROBES. THE MOST INFERIORLY DIRECTED PROBE TIPPROJECTS POSTERIOR TO THE L3 VERTEBRAL BODY NEAR THE INFERIOR ENDPLATE. SUPERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L1 VERTEBRAL BODY NEAR ITS INFERIOR ENDPLATE.; XR OF LUMBAR SPINE: AS BEFORE THERE IS A REMOTE POSTERIOR FUSION FROM L4 THROUGH S1. POSTERIOR SURGICAL RETRACTOR AND SURGICAL DEFECTS. THE SUPERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L1 VERTEBRAL BODY NEAR THE SUPERIOR ENDPLATE. THE MORE INFERIORLY DIRECTED PROBE TIP NOW PROJECTS POSTERIOR TO THE L4 VERTEBRAL BODY NEAR ITS SUPERIOR ENDPLATE.

| | |
|---|---|
| **AE Stopped Rx Day** | 187 |
| **Duration of AE** | 81 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | MEDICAL HISTORY OF SPINAL STENOSIS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | KIDNEY STONE |
| **Preferred term** | 腎結石症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 320 |
| **Age at AE Onset** | 7[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 320): Alanine Aminotransferase: 25 [7 - 52] U/L; Albumin: 39 [35 - 50] G/L; Alkaline Phosphatase: 85 [34 - 104] U/L; Aspartate Aminotransferase: 28 [13 - 39] U/L; Basophils: 0.1 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.4 [0.25 - 1] %; Bilirubin: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Bilirubin: 7 [5 - 17] UMOL/L; Blood: 3+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Blood Urea Nitrogen: 7.1 [2.5 - 8.9] MMOL/L; Calcium: 2.17 [2.15 - 2.57] MMOL/L; Chloride: 107 [98 - 107] MMOL/L; Creatinine: 98 [53 - 106] UMOL/L; Eosinophils: 0.1 [0 - 0.8] 10^9/L; Eosinophils/Leukocytes: 1.3 [0.9 - 2.9] %; Erythrocytes: 10-25 [0 - 2] /HPF; Erythrocytes: 3.8 [4.2 - 5.4] 10^12/L; Glucose: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: 5.6 [4.1 - 6.1] MMOL/L; Hematocrit: 0.36 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 116 [125 - 160] G/L; Ketones: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 0-5 [0 - 5] /HPF; Leukocytes: 8.2 [3.6 - 10.6] 10^9/L; Lymphocytes: 1.4 [1.5 - 3.5] 10^9/L; Lymphocytes/Leukocytes: 16.5 [24 - 44] %; Monocytes: 0.8 [0.1 - 1] 10^9/L; Monocytes/Leukocytes: 9.3 [2.5 - 9] %; NPTST046-ANON GAP: 11 [8 - 17] MEQ/L; NPTST068-APPEARANCE: CLEAR [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST084-BACTERIA: PRESENT [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST176-CO2: 26 [21 - 31] MMOL/L; NPTST182-COLOR: YELLOW [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST205-CREATININE CLEARANCE: 61.77 [NOT REPORTED - NOT REPORTED] ML/MIN; NPTST244-EGFR NON -AA: 48

[60.1 - 100] ML/MIN/1.73M2; NPTST297-GFR AA: 58 [59 - 100] ML/MIN/1.73M2; NPTST360-IG#: 0.06 [0 - 0.1] 10^3/UL; NPTST361-IG%: 0.7 [0 - 3] %; NPTST427-MCH: 30.3 [27 - 32] PG; NPTST428-MCHC: 32.1 [32 - 36] G/DL; NPTST429-MCV: 94.3 [78 - 100] FL; NPTST454-MPV: 8.5 [6 - 11] FL; NPTST474-NRBC %: 0.1 [0 - 0] %; NPTST475-NRBC#: 0.1 [0.03 - 0.12] 10^3/UL; NPTST562-RDW: 16.6 [11.5 - 14] %; NPTST611-SQUAMOUS EPI: 2-5 [0 - 2] /HPF; NPTST694-VOLUME: >7 [NOT REPORTED - NOT REPORTED] ML; Neutrophils: 5.9 [1.3 - 6] 10^9/L; Neutrophils/Leukocytes: 71.8 [36 - 66] %; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 361 [150 - 450] 10^9/L; Potassium: 3.7 [3.4 - 5.1] MMOL/L; Protein: TRACE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 60 [60 - 83] G/L; Sodium: 140 [136 - 145] MMOL/L; Specific Gravity: 1.020 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Urobilinogen: 0.2 [0.2 - 0.2] UNIT NOT REPORTED; pH: 7.5 [7 - 7] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 321): Basophils: 0.03 [NOT REPORTED - 0.08] 10^3/uL; Basophils/Leukocytes: 0.3 [0 - 2] %; Bilirubin: NEGATIVE [NOT REPORTED - NOT REPORTED] NONE PROVIDED; Creatinine: 162 [45 - 84] UMOL/L; Eosinophils: 0.12 [0.04 - 0.36] 10^9/L; Eosinophils/Leukocytes: 1.3 [1 - 4] %; Erythrocytes: 4.3 [3.9 - 5.2] 10^12/L; Glucose: 50 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hematocrit: 0.41 [0.34 - 0.45] FRACTION OF 1; Hemoglobin: 129 [112 - 157] G/L; Ketones: 5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 9.1 [4 - 10] 10^9/L; Lymphocytes: 1.86 [1.18 - 3.74] 10^9/L; Lymphocytes/Leukocytes: 20.6 [20 - 44] %; Monocytes: 0.63 [0.2 - 0.76] 10^9/L; Monocytes/Leukocytes: 7 [2 - 9] %; NPTST014-ABSOLUTE IMMATURE GRANULOCYTE C: 0.05 [NOT REPORTED - 0.05] X10^3/MCL; NPTST015-ABSOLUTE NRBCS: 0.00 [NOT REPORTED - 0.01] X10^3/MCL; NPTST171-CLARITY: SLIGHTLY CLOUDY [NOT REPORTED - NOT REPORTED] NONE PROVIDED; NPTST182-COLOR: YELLOW [NOT REPORTED - NOT REPORTED] NONE PROVIDED; NPTST242-EGFR: 33 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST245-EGFR NON AFRICAN AMERICAN: 27 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST359-IG AUTO: 0.6 [NOT REPORTED - NOT REPORTED] %; NPTST411-LEUKOCYTS ESTERASE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST427-MCH: 30.4 [25.6 - 32.2] PG; NPTST428-MCHC: 31.5 [31 - 34.6] G/DL; NPTST429-MCV: 96.5 [82 - 100.8] FL; NPTST454-MPV: 8.2 [8.97 - 11.96] FL; NPTST473-NRBC: 0 [0 - 0] /100 WBC; NPTST482-OCCULT BLOOD: SMALL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST562-RDW: 16.7 [11.7 - 14.4] %; Neutrophils: 6.36 [1.56 - 6.13] 10^9/L; Neutrophils/Leukocytes: 70.2 [50 - 70] %; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 391 [139 - 379] 10^9/L; Protein: 100 [NOT REPORTED - NOT REPORTED] mg/dL; Specific Gravity: 1.024 [1.003 - 1.035] UNIT NOT REPORTED; Urobilinogen: <2.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; pH: 5 [5 - 9] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 322): Basophils: <0.03 [NOT REPORTED - 0.08] X10^3/MCL; Basophils/Leukocytes: 0.1 [0 - 2] %; Blood Urea Nitrogen: 6.1 [2.5 - 7.9] MMOL/L; Calcium: 2.1 [2.12 - 2.52] MMOL/L; Chloride: 111 [98 - 107] MMOL/L; Creatinine: 96 [45 - 84] UMOL/L; Eosinophils: 0.03 [0.04 - 0.36] 10^9/L; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 3.7 [3.9 - 5.2] 10^12/L; Glucose: 7.4 [3.9 - 5.5] MMOL/L; Hematocrit: 0.36 [0.34 - 0.45] FRACTION OF 1; Hemoglobin: 114 [112 - 157] G/L; Leukocytes: 7.8 [4 - 10] 10^9/L; Lymphocytes: 0.61 [1.18 - 3.74] 10^9/L; Lymphocytes/Leukocytes: 7.8 [20 - 44] %; Monocytes: 0.26 [0.2 - 0.76] 10^9/L; Monocytes/Leukocytes: 3.3 [2 - 9] %; NPTST014-ABSOLUTE IMMATURE GRANULOCYTE C: <0.03 [NOT REPORTED - 0.05] X10^3/MCL; NPTST015-ABSOLUTE NRBCS: 0.00 [NOT REPORTED - 0.01] X10^3/MCL; NPTST044-ANION GAP: 6.0 [4 - 12] UNIT NOT REPORTED; NPTST123-BUN/CR RATIO: 15.6 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST176-CO2: 24 [21 - 32] MMOL/L; NPTST243-EGFR AFRICAN AMERICAN: 59 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST245-EGFR NON AFRICAN AMERICAN: 49 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST359-IG AUTO: 0.3 [NOT REPORTED - NOT REPORTED] %; NPTST427-MCH: 30.5 [25.6 - 32.2] PG; NPTST428-MCHC: 31.8 [31 - 34.6] G/DL; NPTST429-MCV: 95.7 [NOT REPORTED - 100.8] fL; NPTST454-MPV: 8.6 [8.97 - 11.96] FL; NPTST476-NRBCS: 0.0 [NOT REPORTED - NOT REPORTED] /100 (WBCS); NPTST562-RDW: 16.7 [11.7 - 14.4] %; Neutrophils: 6.93 [1.56 - 6.13] 10^9/L; Neutrophils/Leukocytes: 88.5 [50 - 70] %; Platelets: 350 [139 - 379] 10^9/L; Potassium: 4.5 [3.5 - 5.1] MMOL/L; Sodium: 141 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 337): Bilirubin: SMALL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Blood: LARGE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Ketones: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: SMALL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST068-APPEARANCE: CLOUDY [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST182-COLOR: RED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 300 OR GREATER [NOT REPORTED - NOT REPORTED] mg/dL; Specific Gravity: 1.020 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Urobilinogen: 1.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; pH: 7 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

**Microbiology**

[redacted]20[redacted] (RX DAY 320): URINE NPTST211-CULTURE: Negative-25,000 COL/ML3 OR MORE COLONY TYPES, NONE IN PREDOMINANCE, SUSPECTED CONTAMINATION, SUGGEST REPEAT SPECIMEN.; [redacted]20[redacted] (RX

DAY 321): URINE NPTST211-CULTURE: Negative; [redacted]20[redacted] (RX DAY 325): URINE NPTST211-CULTURE: Negative; [redacted]20[redacted] (RX DAY 345): URINE NPTST211-CULTURE: Negative

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 320): CT SCAN: CT SCAN WITHOUT CONTRAST SHOWS MILD TO MODERATE LEFT HYDRONEPHROSIS WITH OBSTRUCTING 5MM STONE IN THE DISTAL URETER.THERE ARE PUNCTATE 1-2MM NONOBSTRUCTING STONES AT THE UPPER AND LOWER POLE OF THE LEFT KIDNEY; [redacted]20[redacted] (RX DAY 321): CT SCAN: THERE IS A 3 TO 4MM OBSTRUCTING KIDNEY STONE IDENTIFIED IN THE LEFT URETHRA WITH MODERATE UPSTREAM HYROURETERNEPHROSIS.; CTSCAN: THERE IS A LEFT SIDED DOUBLE J URETERAL STENT IN PLACE. NO LEFT HYDRONEPHROSIS.; LEFT URETHRAL STENT PLACEMENT: STENT PLACED; [redacted]20[redacted] (RX DAY 337): CYSTOSCOPY WITH STENT REMOVAL: SUCCESSFUL URETERAL STENT REMOVAL AFTER SPONTANEOUS PASSAGE OF STONE.; [redacted]20[redacted] (RX DAY 344): RENAL AND BLADDER ULTRASOUND: TRANSCUTANEOUS IMAGINE WAS PERFORMED OF KIDNEYS AND BLADDER AND NO SIGNIFICANT ABNORMALITY WAS FOUND; [redacted]20[redacted] (RX DAY 359): CYSTOSCOPY WITH BILATERAL RETROGRADE PYELOGRAMS: THE URETHRA WAS WITHOUT LESION OR STRICTURES. THE BLADDER WAS WITHOUT ANY EVIDENCE OF TUMORS. THERE ARE NO CALCULI. THERE WAS A STAGE II CYSTOCELE. THE PREVIOUSLY IDENTIFIED ULCERATED OR ERYTHEMA THISLESION WERE NO LONGER IDENTIFIED. THE BLADDER WALL WAS NORMAL. THE TRIGONE WAS NORMAL AND THE URETERAL ORIFICES WERE ORTHOTOPIC. THEY APPEARED NORMAL. CLEAR EFFLUX WAS NOTED BILATERALLY. NO DISTINCTLESIONS WERE IDENTIFIABLE AND THERE WAS NOTHING THAT WARRANTED A BIOPSY ON THIS EXAM.

| | |
|---|---|
| **AE Stopped Rx Day** | 327 |
| **Duration of AE** | 8 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | NATURALLY PREDISPOSED TO KIDNEY STONE DEVELOPMENT |
| **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:** M15-572

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，既存の脊柱管狭窄症の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 2 箱を 4 年間），L4 及び L5 の融合，変形性関節症，右人工股関節置換，乾癬性関節炎，脊柱管狭窄症，高血圧，膀胱スリング，左膝関節置換及び元飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は既存の脊柱管狭窄症の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，既存の脊柱管狭窄症の悪化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は椎弓切除術のため入院した。病歴及び身体的診察の結果，重度の L2 と L3 の狭窄で，L3 と L4 の椎間肥大及び滑液嚢腫を伴っていた。被験者は背部痛を伴う神経性跛行症状を呈していた。また，L4 の椎弓根に近い L3 と L4 の間の椎間板腔が狭くなっていた。同日，L1～L4 の開放両側椎弓切除術と，L3 及び L4 の滑液嚢腫切除が行われた。L1～L4 の開放両側椎弓切除術及び L3～L4 の滑液嚢腫切除が終了した。被験者の経過は非常に良好で神経根症状はなく，本人もとても良くなったと述べた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤はリドカイン貼付剤であった。

Causality for UPADACITINIB (Blinded)

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1) Spinal column stenosis (10041540) (Spinal stenosis (10082214) ) [v.22.1] [10041540]

**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)

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Event of WORSENING OF PRE-EXISTING SPINAL STENOSIS

**- Investigator:** MEDICAL HISTORY OF SPINAL STENOSIS

**- AbbVie:** EVENT MORE LIKELY RELATED TO PRE-EXISTING SPINAL STENOSIS.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] MRI OF LUMBAR SPINE:** NO ACUTE FRACTURE OR SUBLUXATION. THAT IS POST LUMBAR FUSION FROM L4 THROUGH S1 WITH LAMINECTOMY CHANGES AT L4 AND L5. WHEN COMPARED TO THE PREVIOUS EXAMINATION, DISC DISEASE FROM L1-L2 THROUGH L5-S1 REMAIN STABLE. THERE IS A SLIGHT PROGRESSION OF DISC DISEASE AT T9-T10, T10-T11 AND T11-T12. CENTRAL STENOSIS AT L3-L4 BEING STABLE. FORAMINAL ENCROACHMENT WITH IMPINGEMENT OF THE EXITING RIGHT L3 TO AND L3 NERVE ROOTS REMAIN UNCHANGED.

[redacted] **20[redacted] XR OF LUMBAR SPINE:** AS BEFORE THERE IS A REMOTE POSTERIOR FUSION FROM L4 THROUGH S1. POSTERIOR SURGICAL RETRACTOR AND SURGICAL DEFECTS. THE SUPERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L1 VERTEBRAL BODY NEAR THE SUPERIOR ENDPLATE. THE MORE INFERIORLY DIRECTED PROBE TIP NOW PROJECTS POSTERIOR TO THE L4 VERTEBRAL BODY NEAR ITS SUPERIOR ENDPLATE.

[redacted] **20[redacted] XR OF LUMBAR SPINE:** INTRAOPERATIVE VIEW DEMONSTRATING REMOTE POSTERIOR FUSION FROM L3 THROUGH S1. SURGICAL RETRACTOR IS IN PLACE POSTERIORLY. THERE ARE 2 METALLIC SURGICAL PROBES. THE MOST INFERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L3 VERTEBRAL BODY NEAR THE INFERIOR ENDPLATE. SUPERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L1 VERTEBRAL BODY NEAR ITS INFERIOR ENDPLATE.
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，腎結石の事象を発現した。

**Event 2 の臨床経過：**

関連する病歴は，腎結石症，元喫煙者（1 日 2 箱を 4 年間），糖尿病前症，裂孔ヘルニアによる胃食道逆流性疾患，CK 上昇，変形性関節症，便秘，乾癬性関節炎，コレステロール値上昇，高血圧，膀胱スリング設置，腹圧性尿失禁，尿路感染及び元飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腎結石を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，腎結石は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は病院を受診し，背部痛及び悪心を訴えた。CT スキャン検査で腎結石が見つかった。被験者は麻薬性鎮痛薬を投与されて帰宅した。翌日，被験者は背部痛が悪化したため ED を再受診した。入院となり，CT スキャンの再検査が行われ，鎮痛薬が投与された。腎結石は大きすぎて通過困難と報告された。20[redacted] 年 [redacted] 月 [redacted] 日，左尿道ステントが留置され

た。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，腎結石が自然に通過したため，膀胱鏡下で尿道ステント抜去が行われた。

投与された薬剤は，タムスロシン，オンダンセトロン，ketorolac，生理食塩液，オンダンセトロン，ミダゾラム，ヒドロコルチゾン，セフトリアキソン，アトロピン，シプロフロキサシン，ヒドロコドン・アセトアミノフェン合剤，zofran 及び toradal であった。

Causality for UPADACITINIB (Blinded)

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1) Kidney stone (10023436) (Nephrolithiasis (10029148) ) [v.22.1] [10023436]

**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)

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Event of KIDNEY STONE

**- Investigator:** Naturally predisposed to kidney stone development.

**- AbbVie:** Event is more likely related to pre-existing history of nephrolithiasis. Obesity (BMI 32.8) is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 25 U/L (normal 7 to 52)

[redacted] **20[redacted] ALBUMIN:** 3.9 G/DL (normal 3.5 to 5.0)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 85 U/L (normal 34 to 104)

[redacted] **20[redacted] ANION GAP:** 11 MEQ/L (normal 8 to 17)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 28 U/ML (normal 13 to 39)

[redacted] **20[redacted] BASOPHILS:** 0.40 % (normal 0.25 to 1.00)

[redacted] **20[redacted] BASOPHILS %:** 0.3 %

[redacted] **20[redacted] BASOPHILS ABS:** 0.03 X10**3/MCL (normal <0.08)

[redacted] **20[redacted] BILIRUBIN:** 0.4 mg/dL (normal 0.3 to 1.0)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 20 mg/dL (normal 7 to 25)

**Unknown date BMI:** 32.88646 mg/m2

[redacted] **20[redacted] BUN:** 17 mg/dL (normal >22)

[redacted] **20[redacted] BUN/CREATININE RATIO:** 15.6 mL/min/1.73m2 (Norml >=60)

[redacted] **20[redacted] CALCIUM:** 8.4 mg/dL (normal 8.5 to 10.1)

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

[redacted] **20[redacted] CHLORIDE:** 111 MMOL/L (normal 98 to 107)

[redacted] **20[redacted] CO2:** 26 MMOL/L (normal 21 to 31)

[redacted] **20[redacted] CREATININE:** 1.11 mg/dL (normal 0.60 to 1.20)

[redacted] **20[redacted] CREATININE:** 1.83 mg/dL (normal 0.51 to 0.95)

[redacted] **20[redacted] CREATININE:** 1.09 mg/dL (normal 0.51 to 0.95)

[redacted] **20[redacted] CREATININE CLEARANCE:** 61.77 ML/Min

[redacted] **20[redacted] CT SCAN:** CT SCAN WITHOUT CONTRAST SHOWS MILD TO MODERATE LEFT HYDRONEPHROSIS WITH OBSTRUCTING 5MM STONE IN THE DISTAL URETER.THERE ARE PUNCTATE 1-2MM NONOBSTRUCTING STONES AT THE UPPER AND LOWER POLE OF THE LEFT KIDNEY

[redacted] **20[redacted] CT SCAN:** THERE IS A 3 TO 4MM OBSTRUCTING KIDNEY STONE IDENTIFIED IN THE LEFT URETER WITH MODERATE UPSTREAM HYROURETERNEPHROSIS.

[redacted] **20[redacted] CT SCAN:** THERE IS A LEFT SIDED DOUBLE J URETERAL STENT IN PLACE. NO LEFT HYDRONEPHROSIS.

[redacted] **20[redacted] CYSTOSCOPY:** SUCCESSFUL URETERAL STENT REMOVAL AFTER SPONTANEOUS PASSAGE OF STONE.

[redacted] **20[redacted] EGFR:** 33 mL/min/1.73m2 (Normal >= 60)

[redacted] **20[redacted] EGFR (NON AFRICAN AMERICAN):** 27 mL/min/1.73m2 (Normal >= 60)

[redacted] **20**[redacted] **EGFR AFRICAN AMERICAN:** 59 ¥mL/min/1.73m2 (Normal >= 60)

[redacted] **20**[redacted] **EGFR NON AFRICAN AMERICAN:** 49 mL/min/1.73m2 *Normal >= 60)

[redacted] **20**[redacted] **EOSINOPHILS:** 1.3 % (normal 0.9 to 2.9)

[redacted] **20**[redacted] **EOSINOPHILS %:** 0.0 %

[redacted] **20**[redacted] **GFR AA:** 58 mL/min/1.73m2 (Normal 59 to 100)

[redacted] **20**[redacted] **GLUCOSE:** 101 mg/dL (normal 74 to 109)

[redacted] **20**[redacted] **GLUCOSE:** 134 mg/dL (normal 70 to 99)

[redacted] **20**[redacted] **HEMATOCRIT:** 36.1 % (normal 37.0 to 47.0)

[redacted] **20**[redacted] **HEMATOCRIT:** 41.0 % (normal 34.1 to 44.9)

[redacted] **20**[redacted] **HEMOGLOBIN:** 11.6 G/DL (normal 12.5 to 16.0)

[redacted] **20**[redacted] **HEMOGLOBIN:** 12.9 G/DL (normal 11.2 to 15.7)

[redacted] **20**[redacted] **HEMOGLOBIN:** 11.4 G/DL (normal 11.2 to 15.7)

[redacted] **20**[redacted] **LYMPHOCYTES:** 16.5 % (normal 24.0 to 44.0)

[redacted] **20**[redacted] **LYMPHOCYTES ABS:** 1.4 X10**3/MCL (normal 1.5 to 3.5)

[redacted] **20**[redacted] **LYMPHOCYTES ABS:** 186 10^3/uL (normal 1.18 to 3.74)

[redacted] **20**[redacted] **LYMPHOCYTES ABS:** 0.61 X10**3/MCL (normal 1.18 to 3.74)

[redacted] **20**[redacted] **MONOCYTE ABS:** 0.26 X10**3/MCL (normal 0.20 to 0.76)

[redacted] **20**[redacted] **MONOCYTES:** 9.3 % (normal 2.5 to 9.0)

[redacted] **20**[redacted] **NEUTROPHILS:** 71.8 % (normal 36.0 to 66.0)

[redacted] **20**[redacted] **NEUTROPHILS:** 70.2 % (normal 36.0 to 66.0)

[redacted] **20**[redacted] **NEUTROPHILS %:** 88.5 %

[redacted] **20**[redacted] **NEUTROPHILS ABS:** 6.36 X10**3/MCL (normal 1.56 to 6.13)

[redacted] **20**[redacted] **NEUTROPHILS ABS:** 6.93 X10**3/MCL (normal 1.56 to 6.13)

[redacted] **20**[redacted] **PLATELET COUNT:** 361 X10**3/MCL (normal 150 to 450)

[redacted] **20**[redacted] **PLATELET COUNT:** 391 X10**3/MCL (normal 139 to 379)

[redacted] **20**[redacted] **PLATELET COUNT:** 350 X10**3/MM**3 (normal 139 to 379)

[redacted] 20[redacted] **POTASSIUM:** 3.7 MMOL/L (normal 3.4 to 5.1)

[redacted] 20[redacted] **POTASSIUM:** 4.5 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **PROTEIN:** 6.0 G/DL (normal 6.0 to 8.3)

[redacted] 20[redacted] **RED BLOOD CELLS:** 3.83 X10**6/MCL (normal 4.2 to 5.40)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.25 X10**6/MCL (normal 3.93 to 5.22)

[redacted] 20[redacted] **RED BLOOD CELLS:** 3.74 X10**6/MCL (normal 3.93 to 5.22)

[redacted] 20[redacted] **RENAL AND BLADDER ULTRASOUND:** TRANSCUTANEOUS IMAGINE WAS PERFORMED OF KIDNEYS AND BLADDER AND NO SIGNIFICANT ABNORMALITY WAS FOUND

[redacted] 20[redacted] **SODIUM:** 140 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] **SQUAMOUS EPI (URINE):** 2-5 HPF (normal 0-2 /HPF)

[redacted] 20[redacted] **URINE APPEARANCE:** Clear

[redacted] 20[redacted] **URINE APPEARANCE:** CLOUDY/RED

[redacted] 20[redacted] **URINE BACTERIA:** Present

[redacted] 20[redacted] **URINE BILIRUBIN:** Negative

[redacted] 20[redacted] **URINE BILIRUBIN:** Negative

[redacted] 20[redacted] **URINE BILIRUBIN:** SMALL

[redacted] 20[redacted] **URINE BLOOD:** 3+ (normal = negative)

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

[redacted] 20[redacted] **URINE CLARITY:** slightly cloudy

[redacted] 20[redacted] **URINE COLOR:** Yellow

[redacted] 20[redacted] **URINE COLOR:** Yellow

[redacted] 20[redacted] **URINE CULTURE:** 25,000 COL/ML3 OR MORE COLONY TYPES, NONE IN PREDOMINANCE, SUSPECTED CONTAMINATION, SUGGEST REPEAT SPECIMEN

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

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

[redacted] 20[redacted] **URINE CULTURE:** NEGATIVE

[redacted] 20[redacted] **URINE GLUCOSE:** Negative

[redacted] **20[redacted] URINE GLUCOSE:** 50 no unit

[redacted] **20[redacted] URINE GLUCOSE:** NEGATIVE

[redacted] **20[redacted] URINE KETONES:** Negative

[redacted] **20[redacted] URINE KETONES:** 5 no unit

[redacted] **20[redacted] URINE KETONES:** NEGATIVE

[redacted] **20[redacted] URINE LEUKOCYTES:** Negative

[redacted] **20[redacted] URINE LEUKOCYTES ESTERASE:** Negative

[redacted] **20[redacted] URINE NITRITE:** Negative

[redacted] **20[redacted] URINE NITRITE:** Negative

[redacted] **20[redacted] URINE NITRITE:** NEGATIVE

[redacted] **20[redacted] URINE OCCULT BLOOD:** Small (normal = negative)

[redacted] **20[redacted] URINE PH:** 7.5 no units (normal 7.0 to 7.0)

[redacted] **20[redacted] URINE PH:** 5 no units (normal 5 to 9)

[redacted] **20[redacted] URINE PH:** 7 NO UNITS

[redacted] **20[redacted] URINE PROTEIN:** Trace (normal = negative)

[redacted] **20[redacted] URINE PROTEIN:** 100 mg/dL

[redacted] **20[redacted] URINE PROTEIN:** 300MG/DL OR GREATER

[redacted] **20[redacted] URINE RBC:** 10-25 /HPF (normal >=0 to <=2)

[redacted] **20[redacted] URINE SPECIFIC GRAVITY:** 1.020 no units (normal 1.003 to 1.035)

[redacted] **20[redacted] URINE SPECIFIC GRAVITY:** 1.024 no units (normal 1.003 to 1.035)

[redacted] **20[redacted] URINE SPECIFIC GRAVITY:** 1.020 NO UNIT

[redacted] **20[redacted] URINE UROBILINOGRN:** 1.0 NO UNITS

[redacted] **20[redacted] URINE UROBILIRUBIN:** 0.2 no units (normal 0.2 to 0.2)

[redacted] **20[redacted] URINE UROBILIRUBIN:** <2.0 (Normal <= 2.0

[redacted] **20[redacted] URINE VOLUME:** >7 mL

[redacted] **20[redacted] URINE WBC:** 0-5 /HPF (Normal >= 0 to <= 5)

[redacted] **URINE WHITE BLOOD CELLS:** SMALL

[redacted] **WHITE BLOOD CELLS:** 8.2 X10**3/MCL (normal 3.6 to 10.6)

[redacted] **WHITE BLOOD CELLS:** 9.05 X10**3/MCL (normal 3.98 to 10.04)

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 |
|---|---|---|---|---|
| 腸膀胱瘻 | X | | | X |

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

| Medical History | Onset Year |
|---|---|
| OTHER: PLAQUE PSORIASIS | 19[redacted] |
| HYPERTENSION: WHITE COAT SYNDROME | 19[redacted] |
| OTHER: HYPERCHOLESTEROLEMIA | 19[redacted] |
| OTHER: POLYCYTHEMIA - RESOLVED WHEN QUIT SMOKING | 20[redacted] |
| OTHER: PREDIABETES | 20[redacted] |
| OTHER: FORMER CIGARETTE SMOKER | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| CARDIAC ARRHYTHMIA: BIGEMINY | 20[redacted] |
| CARDIAC ARRHYTHMIA: PREMATURE VENTRICULAR BEATS | 20[redacted] |
| CORONARY ARTERY DISEASE: CAD IN NATIVE ARTERY | 20[redacted] |
| MYOCARDIAL INFARCTION | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: NEUROFIBROMA OF THORACIC REGION | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 2 PACK | 35 | 20[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | 2 - 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 169 | 169 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 170 | [redacted]20[redacted] / 393 | 224 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 394 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| LISINOPRIL | 5 mg | BID | Y-M: 19[redacted] |
| COLECALCIFEROL | 1,000 OTHER: UNIT | QD | Y-M: 19[redacted] |
| ASCORBIC ACID | 1000 mg | QD | Y-M: 20[redacted] |
| BETAMETHASONE | 1 OTHER: APPLICATION | QD | Y-M: 20[redacted] |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] |
| ROSUVASTATIN | 10 mg | QD | Y-M: 20[redacted] |
| HERPES ZOSTER 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 |
|---|---|---|---|---|
| LISINOPRIL | 5 mg | BID | Y-M: 19[redacted] | NOT REPORTED |
| COLECALCIFEROL | 1,000 OTHER: UNIT | QD | Y-M: 19[redacted] | NOT REPORTED |
| ASCORBIC ACID | 1000 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| ROSUVASTATIN | 10 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] / 487 | Y-M: 20[redacted] / 520 |
| BETAMETHASONE | 1 OTHER: APPLICATION | PRN | Y-M: 20[redacted] / 502 | NOT REPORTED |
| BUPIVACAINE | 20 mL | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| DEXAMETHASONE | 4 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| DIPHENHYDRAMINE | 12.5 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| FENTANYL | 100 ug | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| FLEBOBAG RING LACT | 1100 mL | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| GLYCOPYRRONIUM | 0.8 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| KETAMINE | 40 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| LIDOCAINE | 80 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| MAGNESIUM | 2 g | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| MIDAZOLAM | 2 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| NEOSTIGMINE | 5 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |

| | | | | |
|---|---|---|---|---|
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| PROPOFOL | 200 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| ROCURONIUM | 90 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 515 |
| HYDROMORPHONE | 0.5 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 516 |
| OXYCODONE | 5 mg | PRN | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 517 |
| SODIUM CHLORIDE | 5 mL | BID | Y-M: 20[redacted] / 515 | Y-M: 20[redacted] / 520 |

**Event #1: Serious Adverse Event, Event of Interest - Gastrointestinal Perforations**

| | |
|---|---|
| **Event Description** | COLOVESICAL FISTULA |
| **Preferred term** | 腸膀胱瘻 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 483 |
| **Age at AE Onset** | 7[redacted] |

**Laboratory Testing**
NOT REPORTED
**Microbiology**
NOT REPORTED
**SAE Supplemental Procedure**
[redacted]20[redacted] (RX DAY 515): LAPAROSCOPIC COLECTOMY, PARTIAL, W/ANAST. W/COLOPROCTOSTOMY (LOW PELVIC ANAST. (: SUCCESSFUL TAKEDOWN OF COLOVESICULAR FISTULA

| | |
|---|---|
| **AE Stopped Rx Day** | 515 |
| **Duration of AE** | 33 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | DIVERTICULOSIS |
| **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:** M15-572

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，結腸膀胱瘻の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，局面型乾癬，高コレステロール血症，赤血球増加症（禁煙で消失した），糖尿病前症，乾癬性関節炎，元喫煙者（1 日 2 箱を 35 年間）及び現飲酒者（1 日 2～4 杯）であ

った。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は結腸膀胱瘻を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，結腸膀胱瘻は消失した。

被験者は反復性尿路感染症（非重篤）のため泌尿器科で精密検査を受けることになった。被験者は CT スキャン検査を受け，腸管と膀胱の間の結腸膀胱瘻及び憩室症（非重篤）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，腹腔鏡下結腸部分切除術を受け，結腸直腸吻合術による吻合（低位骨盤吻合）が行われた。手術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

**The patient's past medications include:**

DIPROLENE CREAM 0.05% for PSORIASIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

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

Causality for UPADACITINIB (Blinded)

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1) Colovesical fistula (10010066) (Enterovesical fistula (10062570) ) [v.23.0] [10010066]

**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 COLOVESICAL FISTULA

**- Investigator:** DIVERTICULOSIS

**- AbbVie:** Event is more likely a complication of concurrent diverticulosis( as seen per CT). Additional risk factors include elderly age and male gender.

Relevant Laboratory & Other Diagnostic Tests

---

**20[redacted] CT SCAN:** Colovesicular fistula. Small 3 mm fistulous tract between distal sigmoid colon and mid bladder, left-sided diverticulosis (non serious).

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 |

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

| Medical History | Onset Year |
|---|---|
| OTHER: PERIODICALLY EXPERIENCES SYMPTOMS OF SCIATICA | 19[redacted] |
| OTHER: PLAQUE PSORIASIS | 19[redacted] |
| OTHER: REACTIVE AIRWAY DISEASE | 20[redacted] |
| OTHER: SEASONAL ALLERGIES | 20[redacted] |
| OTHER: PLANTAR FASCIAL FIBROMATOSIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| HYPERTENSION: DIAGNOSIS PRIOR TO 1ST DOSE OF I.P. ICF SIGNED 07SEP2017 | 20[redacted] |
| ANGINA: PRINZMETAL'S ANGINA | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: NASAL SURGERY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | FORMER | | | |
| CIGARETTES | FORMER | 0.5 PACK | 5 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

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

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MONTELUKAST | 10.00 mg | QD | Y-M: 20[redacted] |
| PROCATEROL | 90 OTHER: MCG | PRN | Y-M: 20[redacted] |
| SERETIDE | 250.0 OTHER: MCG | PRN | Y-M: 20[redacted] |
| FOLIC ACID | 1.00 mg | QD | Y-M: 20[redacted] |
| METHOTREXATE | 25.00 mg | EVERY WEEK | Y-M: 20[redacted] / -116 |
| ACETYLSALICYLIC ACID | 81.00 mg | QD | Y-M: 20[redacted] / -11 |
| AMLODIPINE | 5.00 mg | QD | Y-M: 20[redacted] / -11 |
| ATORVASTATIN | 40.00 mg | QD | Y-M: 20[redacted] / -11 |
| CLOPIDOGREL | 75.00 mg | QD | Y-M: 20[redacted] / -11 |
| GLYCERYL TRINITRATE | 0.40 mg | QD | Y-M: 20[redacted] / -11 |

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

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MONTELUKAST | 10.00 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| SERETIDE | 250.0 OTHER: MCG | PRN | Y-M: 20[redacted] | NOT REPORTED |
| FOLIC ACID | 1.00 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 606 |
| METHOTREXATE | 25.00 mg | EVERY WEEK | Y-M: 20[redacted] / -116 | Y-M: 20[redacted] / 606 |
| ACETYLSALICYLIC ACID | 81.00 mg | QD | Y-M: 20[redacted] / -11 | NOT REPORTED |
| VERAPAMIL | 240.00 mg | QD | Y-M: 20[redacted] / 40 | Y-M: 20[redacted] / 606 |
| AMLODIPINE | 5 mg | QD | Y-M: 20[redacted] / 58 | NOT REPORTED |
| ROSUVASTATIN | 5.00 mg | OTHER: QOD | Y-M: 20[redacted] / 58 | NOT REPORTED |
| HYDROCHLOROTHIAZIDE | 25 mg/m2 | QD | Y-M: 20[redacted] / 312 | Y-M: 20[redacted] / 604 |
| POTASSIUM | 20 mg | QD | Y-M: 20[redacted] / 606 | Y-M: 20[redacted] / 607 |
| LEVOFLOXACIN | 750 mg | QD | Y-M: 20[redacted] / 607 | Y-M: 20[redacted] / 612 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / 607 | Y-M: 20[redacted] / 612 |

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

| | |
|---|---|
| **Event Description** | GASTROENTERITIS |
| **Preferred term** | 胃腸炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 602 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **SAE Supplemental Procedure** | |
| NOT REPORTED | |
| **AE Stopped Rx Day** | 608 |
| **Duration of AE** | 7 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |

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

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，胃腸炎の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，元紙巻タバコ喫煙者（1 日 0.5 箱を 5 年間），乾癬性関節炎，高血圧，元噛みタバコ使用者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

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，胃腸炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，嘔吐，発熱，難治性下痢及び脱水で来院した。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，塩化カリウム，メトロニダゾール及びレボフロキサシンであった。

Causality for UPADACITINIB (Blinded)

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1) Gastroenteritis (10017888) (Gastroenteritis (10017888) ) [v.22.1] [10017888]

**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 GASTROENTERITIS

**- Investigator:** Not applicable

**- AbbVie:** Event is common in the general population.

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 |
|---|---|---|---|---|
| 椎間板変性症 | X | | | |
| 脊椎後方すべり症 | X | | | |

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

| Medical History | Onset Year |
|---|---|
| DEGENERATIVE DISC DISEASE | 19[redacted] |
| OTHER: PLAQUE PSORIASIS | 19[redacted] |
| OTHER: ANXIETY | 20[redacted] |
| HYPERLIPIDEMIA | 20[redacted] |
| OTHER: HYPERTENSION | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: SLEEP APNEA | 20[redacted] |
| GASTROESOPHAGEAL REFLUX DISEASE: GASTROESOPHAGEAL REFLUX DISORDER | 20[redacted] |

| Prior Procedures | | Procedure Year |
|---|---|---|
| SURGERY: LUMBAR SPINE DISCECTOMY | DEGENERATIVE DISC DISEASE | 19[redacted] |
| SURGERY: LEFT ROTATOR CUFF REPAIR | | 19[redacted] |
| SURGERY: CERVICAL SPINE FUSION | DEGENERATIVE DISC DISEASE | 20[redacted] |
| SURGERY: INGUINAL HERNIA | | 20[redacted] |
| SURGERY: LEFT ROTATOR CUFF REPAIR | | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 10 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 168 | 168 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 169 | [redacted]20[redacted] / 390 | 222 |

| | | | | |
|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 391 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| LORAZEPAM | 2 mg | OTHER: QHS | Y-M: 20[redacted] |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] |
| ENALAPRIL | 20 mg | QD | Y-M: 20[redacted] |
| LEFLUNOMIDE | 20 mg | QD | Y-M: 20[redacted] |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] |
| VICODIN | 7.5 mg | BID | Y-M: 20[redacted] / -298 |

**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 |
|---|---|---|---|---|
| LORAZEPAM | 2 mg | OTHER: QHS | Y-M: 20[redacted] | NOT REPORTED |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| ENALAPRIL | 20 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| VICODIN | 7.5 mg | BID | Y-M: 20[redacted] / -298 | NOT REPORTED |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | DEGENERATIVE DISC DISEASE WITH RETROLISTHESIS |
| **Preferred term** | 椎間板変性症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 504 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 504): L5-S1 TRANSFORAMINAL LUMBAR INTERBODY FUSION: RESOLVED

| | |
|---|---|
| **AE Stopped Rx Day** | 507 |
| **Duration of AE** | 4 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | LIFESTYLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | DEGENERATIVE DISC DISEASE WITH RETROLISTHESIS |
| **Preferred term** | 脊椎後方すべり症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 504 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

NOT REPORTED
**Microbiology**
NOT REPORTED
**SAE Supplemental Procedure**
[redacted]20[redacted] (RX DAY 504): L5-S1 TRANSFORAMINAL LUMBAR INTERBODY FUSION: RESOLVED

| | |
|---|---|
| **AE Stopped Rx Day** | 507 |
| **Duration of AE** | 4 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | LIFESTYLE |
| **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:** M15-572

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，後方すべり症を伴う椎間板変性疾患の事象を発現した。

**Event 1 及び 2 の臨床経過：**

関連する病歴は，椎間板変性疾患に対する腰椎椎間板切除術，元喫煙者（1 日 1 箱を 10 年間），左肩回旋筋腱板修復術，局面型乾癬，椎間板変性疾患に対する頚椎融合術，高血圧，乾癬性関節炎，左肩回旋筋腱板修復術及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は後方すべり症を伴う椎間板変性疾患を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，後方すべり症を伴う椎間板変性疾患は消失した。

被験者は長年にわたって腰椎の痛み及びこわばり感を患っていた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，L5～S1 の経椎間孔的腰椎椎体間固定術を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し

た。医療記録は本報告時点で未入手であった。

**The patient's past medications include:**

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

Causality for UPADACITINIB (Blinded)

---

1) Spinal retrolisthesis (10081602) (Spinal retrolisthesis (10081602) ) [v.22.1] [10081602]

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

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

**Dechallenge:** Not Applicable

2) Degenerative disc disease (10070241) (Intervertebral disc degeneration (10061246) ) [v.22.1] [10070241]

**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 DEGENERATIVE DISC DISEASE WITH RETROLISTHESIS

**- Investigator:** Lifestyle

**- AbbVie:** Risk factors include prior history of lumbar spine discectomy, pre-existing psoriatic arthritis and obesity.

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 |
|---|---|---|---|---|
| 遠隔転移を伴う肺癌 | X | X | X | X |

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

| Medical History | Onset Year |
|---|---|
| OTHER: PLAQUE PSORIASIS | NOT REPORTED |
| GASTROESOPHAGEAL REFLUX DISEASE | 19[redacted] |
| DIABETES MELLITUS | 20[redacted] |
| OTHER: SEASONAL ALLERGIES | 20[redacted] |
| HYPERLIPIDEMIA | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| Not reported. | |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 50 | 20[redacted] |
| CIGARS | CURRENT | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 170 | 170 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 171 | [redacted]20[redacted] / 246 | 76 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ATORVASTATIN | 10 mg | QD | Y-M: 20[redacted] / -208 |
| METFORMIN | 500 mg | BID | Y-M: 20[redacted] / -208 |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] / -208 |
| SULFASALAZINE | 500 mg | QD | Y-M: 20[redacted] / -208 |

| | | | |
|---|---|---|---|
| VICODIN | 5-325 mg | PRN | Y-M: 20[redacted] / -208 |
| FOLIC ACID | 2 mg | QD | Y-M: 20[redacted] / -181 |
| METHOTREXATE | 25 mg | EVERY WEEK | Y-M: 20[redacted] / -181 |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] / -125 |
| MAGNESIUM | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -125 |

**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 / Stop Year-Month / RX Day | RX Day |
|---|---|---|---|---|
| ATORVASTATIN | 10 mg | QD | Y-M: 20[redacted] / -208 | ONGOING |
| METFORMIN | 500 mg | BID | Y-M: 20[redacted] / -208 | ONGOING |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] / -208 | ONGOING |
| SULFASALAZINE | 500 mg | QD | Y-M: 20[redacted] / -208 | ONGOING |
| VICODIN | 5-325 mg | PRN | Y-M: 20[redacted] / -208 | ONGOING |
| FOLIC ACID | 2 mg | QD | Y-M: 20[redacted] / -181 | ONGOING |
| METHOTREXATE | 25 mg | EVERY WEEK | Y-M: 20[redacted] / -181 | ONGOING |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] / -125 | ONGOING |
| MAGNESIUM | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -125 | ONGOING |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Death, Event of Interest - Possible Malignancy, Event of Interest - Malignancy, Event of Interest - Malignancy excluding**

| | |
|---|---|
| **Event Description** | LUNG CANCER - LEFT KIDNEY & LIVER METASTASIZE |
| **Preferred term** | 遠隔転移を伴う肺癌 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 239 |
| **Age at AE Onset** | 7[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **SAE Supplemental Procedure** | |
| NOT REPORTED | |
| **AE Stopped Rx Day** | 313 (67 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 75 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, RESULTS IN DEATH |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，致死的な肺癌，左腎・肝転移の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，糖尿病，高脂血症，乾癬性関節炎，元喫煙者（1 日 1 箱を 50 年間），局面型乾癬，現飲酒者（1 日 2 杯未満）及び現葉巻喫煙者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺癌，左腎・肝転移を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死因は肺癌，左腎・肝転移と報告された。剖検が実施されたかどうかは不明である。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は息切れを来し，CT スキャン検査及び呼吸器の治療のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，本事象によりこの被験者の治験は中止された。

Causality for UPADACITINIB (Blinded)

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1) Lung cancer metastatic (10050017) (Lung cancer metastatic (10050017) ) [v.22.0] [10050017]

**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 LUNG CANCER, LEFT KIDNEY AND LIVER METASTASIZE

**- Investigator:** Not applicable

**- AbbVie:** Risk factors include smoking history of 1 PPD for 50 years and advanced age.

Relevant Laboratory & Other Diagnostic Tests

---

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

**[redacted] 20[redacted] CT SCAN:** Not reported

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 |
|---|---|---|---|
| Placebo to UPA 15 mg QD | 4[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| SYNCOPE: NEUROCARDIOGENIC SYNCOPE | 19[redacted] |
| OTHER: PLAQUE PSORIASIS | 19 |
| MIGRAINE HEADACHE | 19 |
| DEPRESSION: BIPOLAR DEPRESSION | 19 |
| OBESITY | 19 |
| OTHER: ANXIETY | 19 |
| GASTROESOPHAGEAL REFLUX DISEASE | 19 |
| OTHER: URINARY INCONTINENCE | 20 |
| OTHER: CENTRALIZED BODY PAIN | 20 |
| OTHER: SYNOVITIS | 20 |
| ASTHMA | 20 |
| PSORIATIC ARTHRITIS | 20 |
| OTHER: UNSPECIFIED NONTOXIC NODULAR GOITER | 20 |
| HYPERTENSION | 20 |
| OTHER: DEEP VEIN THROMBOSIS | 20 |
| OTHER: PRE-DIABETES MELLITUS | 20 |
| OTHER: INSOMNIA | 20 |
| OTHER: MUSCLE SPASMS | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: VERTICAL BANDED GASTROPLASTY | 19[redacted] |
| SURGERY: TUBAL LIGATION | 20 |
| SURGERY: C-SECTION | 20 |
| SURGERY: TOTAL HYSTERECTOMY | 20 |
| SURGERY: RIGHT KNEE MENISCAL REPAIR | 20 |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | CURRENT | 0.25 PACK | 12 | |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted] / 1 | [redacted] / 179 | 179 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 180 | [redacted] / 395 | 216 |
| ABT-494 | 15 MG | ORAL | QD | [redacted] / 396 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| OMEPRAZOLE | 20 mg | QD | Y-M: 19[redacted] |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] |
| OXYBUTYNIN | 5 mg | QD | Y-M: 20[redacted] |
| IBUPROFEN | 200 mg | PRN | Y-M: 20[redacted] |
| SALBUTAMOL | 90 ug | PRN | Y-M: 20[redacted] |
| SULFASALAZINE | 1500 mg | TID | Y-M: 20[redacted] |
| BUSPIRONE | 30 mg | QD | Y-M: 20[redacted] |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] |
| TIZANIDINE | 4 mg | OTHER: Q6 HOURS | Y-M: 20[redacted] |
| TOPIRAMATE | 100 mg | QD | Y-M: 20[redacted] |
| ZOLPIDEM | 10 mg | PRN | Y-M: 20[redacted] |
| VARENICLINE | 0.5 mg | QD | Y-M: 20[redacted] / -92 |

**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 |
|---|---|---|---|---|
| OMEPRAZOLE | 20 mg | QD | Y-M: 19[redacted] | Y-M: 20[redacted] / 120 |
| OXYBUTYNIN | 5 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 120 |
| IBUPROFEN | 200 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| SALBUTAMOL | 90 ug | PRN | Y-M: 20[redacted] | NOT REPORTED |
| BUSPIRONE | 30 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 301 |
| CITALOPRAM | 40 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 301 |
| TIZANIDINE | 4 mg | OTHER: Q6 HOURS | Y-M: 20[redacted] | NOT REPORTED |
| ZOLPIDEM | 10 mg | PRN | Y-M: 20[redacted] | NOT REPORTED |
| TOPIRAMATE | 100 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 211 |
| VARENICLINE | 0.5 mg | QD | Y-M: 20[redacted] / -92 | Y-M: 20[redacted] / 362 |
| LEVOFLOXACIN | 750 mg | QD | Y-M: 20[redacted] / 60 | Y-M: 20[redacted] / 63 |
| AZITHROMYCIN | 250 mg | OTHER: ONCE | Y-M: 20[redacted] / 63 | Y-M: 20[redacted] / 63 |
| AZTREONAM | 1 g | OTHER: ONCE | Y-M: 20[redacted] / 63 | Y-M: 20[redacted] / 63 |
| VANCOMYCIN | 1000 mg | OTHER: ONCE | Y-M: 20[redacted] / 63 | Y-M: 20[redacted] / 63 |
| SODIUM CHLORIDE | 2 L | OTHER: ONCE | Y-M: 20[redacted] / 63 | Y-M: 20[redacted] / 64 |
| DOXYCYCLINE | 100 mg | BID | Y-M: 20[redacted] / 65 | Y-M: 20[redacted] / 70 |

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

| | |
|---|---|
| **Event Description** | PNEUMONIA |
| **Preferred term** | 肺炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 60 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 63): Leukocytes: 6.8 [4 - 10] 10^9/L; NPTST129-C-REACTIVE PROTEIN: 6.4 [0 - 0.6] MG/DL; NPTST524-PROCALCITONIN: 0.04 [0 - 0.25] NG/ML; NPTST571-RESPIRATORY PATHOGEN PANEL: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 64): NPTST082-B-TYPE NATRUIRETIC PEPTIDE: 106 [0 - 100] PG/ML; NPTST408-LEGIONELLA PNEUMOPHILA ANTIGEN: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST615-STEP PNEUMONIA ANTIGEN: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 65): Leukocytes: 6.3 [4 - 10] 10^9/L

**Microbiology**

[redacted]20[redacted] (RX DAY 63): OTHER NASOPHARYNGEAL SWAB NPTST572-RESPIRATORY PCR PANEL: Negative; [redacted]20[redacted] (RX DAY 64): SPUTUM NPTST027-AEROBIC RESPIRATORY CULTURE: Negative; URINE NPTST408-LEGIONELLA PNEUMOPHILA ANTIGEN: Negative; URINE NPTST616-STREP PNEUMONIA ANTIGEN: Negative; [redacted]20[redacted] (RX DAY 65): SPUTUM NPTST570-RESPIRATORY GRAM STAIN CULTURE: Negative

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 63): CHEST XRAY: 1. INTERVAL DEVELOPMENT OF PATCHY AIRSPACE OPACITY IN THE LEFT MIDLUNG THAT MAY BE INFECTIOUS IN ETIOLOGY. 2. NO DISPLACED RIB OR CLAVICULAR FRACTURES. 3. UNREMARKABLE CARDIAC AND MEDIASTINAL CONTOURS. NO PLEURAL EFFUSION OR PNEUMOTHORAX.; CT ANGIO CHEST WITH CONTRAST- PULMONARY EMBOLISM PROTOCOL: 1. NO PULMONARY EMBOLISM. 2. SUPERIOR SEGMENT LEFT LOWER LOBE PNEUMONIA. 3. MOSAIC ATTENUATION OF THE LUNGS, WHICH MAY RELATE TO SMALL AIRWAYS DISEASE.; [redacted]20[redacted] (RX DAY 64): ECHOCARDIOGRAM: NORMAL LEFT VENTRICULAR DIASTOLIC FUNCTION. NO EVIDENCE OF RIGHT-TO-LEFT SHUNT BY IV SALINE CONTRAST STUDY. TECHNICALLY DIFFICULT STUDY DUE TO BODY HABITUS. CONCLUSIONS ---------- NORMAL OVERALL LEFT VENTRICULAR SYSTOLIC FUNCTION. NORMAL OVERALL RIGHT VENTRICULAR SYSTOLIC FUNCTION.

| | |
|---|---|
| **AE Stopped Rx Day** | 65 |
| **Duration of AE** | 6 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | LIKELY COMMUNITY ACQUIRED PNEUMONIA. |
| **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:** M15-572

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，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，喘息，乾癬性関節炎，高血圧，肺気腫／慢性閉塞性肺疾患，現喫煙者（1 日 0.25 箱を 12 年間）及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

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，20[redacted] 年 [redacted] 月 [redacted] 日の起床時，中背部周囲に放射状に拡がる左乳房の痛みを自覚した。起き上がって少し歩いたところで息切れがし，一過性の頭部ふらふら感と疲労が出現した。この痛みは深く息を吸うと悪化した。被験者は乾癬性関節炎のためすでにリウマチ科に予約を入れていた。胸部 X 線検査が行われ，左肺中葉肺炎の可能性が示唆された。Levaquin 750 mg/日 5 日間の投与が開始された。被験者によれば，発熱はなかったが，悪寒があった。20[redacted] 年 [redacted] 月 [redacted] 日，右上唇に熱性疱疹が出現した。疱疹は痂皮化し，時折透明の滲出液が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，1 日 2 回程度の一過性（持続時間 15～20 分）の悪心を伴う右上腹部痛が出現した。また，左腱痛も出現し，動くと悪化したが，うずくような痛みが絶えずあった。被験者によると，姉妹の 1 人が気管支炎を発症していた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は ER を受診し，息切れ，腹痛，疲労増加，頭部ふらふら感及び悪心を訴えた。肺塞栓症が懸念されたため，胸部 CT 検査が行われたが，肺塞栓症は認められなかった。しかし，左肺下葉上区の肺炎が明らかとなった。被験者は ER 受診時に Levaquin を 4 日間服用していたが，これは静注抗生物質に切り替えられた。20[redacted] 年 [redacted] 月 [redacted] 日，息切れのため，被験者は入院し，緊急検査を受けることとなった。治験責任医師によると，喘息，COPD 及び現喫煙者が関連のある危険因子であった。心エコー検査が行われた。結果は，駆出率 70%で異常なし，B 型ナトリウム利尿ペプチド（BNP）がごくわずかに増加していた。プロカルシトニン値は本事象の持続期間を通して正常であった。20[redacted] 年 [redacted] 月 [redacted] 日，白血球増加症は認められず，息切れも消失し，被験者はドキシサイクリン 100 mg bid 5 日間を処方されて退院した。抗生物質の投与期間終了後，被験者より，症状は消失したと報告された。

投与された薬剤は，azithromax，アズトレオナム，バンコマイシン，ドキシサイクリン及び levaquin であった。

Causality for UPADACITINIB (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664) ) [v.22.1] [10035664]

**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 PNEUMONIA

**- Investigator:** Likely community acquired pneumonia.

**- AbbVie:** Event more likely related to current smoking status and COPD. The investigator reports a risk factor of COPD, which is very likely due to subject's smoking history.

Relevant Laboratory & Other Diagnostic Tests

---

**[redacted] 20[redacted] AEROBIC RESPIRATORY CULTURE (SPUTUM):** negative

**[redacted] 20[redacted] B-TYPE NATRIURETIC PEPTIDE:** 106 PG/ML (normal 0 to 100)

**[redacted] 20[redacted] C-REACTIVE PROTEIN:** 6.4 mg/dL (normal 0.0 to 0.6)

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

**[redacted] 20[redacted] CHEST X-RAY:** possible left middle lobe pneumonia

**[redacted] 20[redacted] CHEST XRAY:** 1. INTERVAL DEVELOPMENT OF PATCHY AIRSPACE OPACITY IN THE LEFT MIDLUNG THAT MAY BE INFECTIOUS IN ETIOLOGY. 2. NO DISPLACED RIB OR CLAVICULAR FRACTURES. 3. UNREMARKABLE CARDIAC AND MEDIASTINAL CONTOURS. NO PLEURAL EFFUSION OR PNEUMOTHORAX.

**[redacted] 20[redacted] CT ANGIO CHEST WITH CONTRAST-PULMONARY EMBOLISM PROTOCOL:** 1. No pulmonary embolism. 2. Superior segment left lower lobe pneumonia. 3. Mosaic attenuation of the lungs, which may relate to small airways disease

**[redacted] 20[redacted] ECHOCARDIOGRAM:** Normal left ventricular diastolic function. No evidence of right-to-left shunt by iv saline contrast study. Technically difficult study due to body habitus. Conclusions: Normal overall left ventricular systolic function. Normal overall right ventricular systolic function. Ejection fraction of 70%

**[redacted]20[redacted] LEGIONELLA PNEUMOPHILA ANTIGEN (URINE):** negative

**[redacted]20[redacted] PROCALCITONIN:** 0.04 ng/mL (normal 0.00 to 0.25)

**[redacted]20[redacted] RESPIRATORY PATHOGEN PANEL:** NASOPHARYNGEAL SWAB: negative

**[redacted]20[redacted] STREP PNEUMONIA ANTIGEN (URINE):** negative

**[redacted]20[redacted] WBC:** 6.8 K/UL (normal 4.0 to 10.0)

**[redacted]20[redacted] WBC:** 6.3 K/UL (normal 4.0 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 |
|---|---|---|---|---|
| インフルエンザ | X | | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 15 mg QD | 3[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: PSORIATIC LESIONS | 20[redacted] |
| DIABETES MELLITUS: TYPE 1 | 20 |
| OTHER: THYROID GOITER | 20 |
| OTHER: PANIC ATTACKS | 20 |
| OTHER: HYPERCHOLESTEROLEMIA | 20 |
| DEPRESSION: ADJUSTMENT DISORDER | 20 |
| OTHER: SINUS TACHYCARDIA | 20 |
| OTHER: SLEEP DISORDER | 20 |
| OTHER: ARTHROPATHIC PSORIASIS | 20 |
| PSORIATIC ARTHRITIS | 20 |
| OTHER: DE QUERVAIN'S DISEASE (RADIAL STYLOID TENOSYNOVITIS) | 20 |
| OTHER: WRIST AND THUMB PAIN | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: GALLBLADDER REMOVED | 20[redacted] |

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

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 169 | 169 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 170 | [redacted]20[redacted] / 221 | 52 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| INSULIN GLARGINE | 100 OTHER: UNITS | BID | Y-M: 20[redacted] |
| INSULIN LISPRO | 100 OTHER: UNITS | PRN | Y-M: 20[redacted] |
| SERTRALINE | 100 mg | QD | Y-M: 20[redacted] |
| PARACETAMOL | 325 MG mg | PRN | Y-M: 20[redacted] |
| ZOLPIDEM | 10 mg | QD | Y-M: 20[redacted] |
| EZETIMIBE | 10 mg | QD | Y-M: 20[redacted] |
| MELOXICAM | 15 MG mg | QD | Y-M: 20[redacted] / -278 |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -259 |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] / -259 |
| TRIAMCINOLONE | 0.025% % | PRN | Y-M: 20[redacted] / -259 |
| ATORVASTATIN | 40 mg | QD | Y-M: 20[redacted] / -132 |

**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 |
|---|---|---|---|---|
| INSULIN GLARGINE | 100 OTHER: UNITS | BID | Y-M: 20[redacted] | ONGOING |
| INSULIN LISPRO | 100 OTHER: UNITS | PRN | Y-M: 20[redacted] | ONGOING |
| SERTRALINE | 100 mg | QD | Y-M: 20[redacted] | ONGOING |
| PARACETAMOL | 325 MG mg | PRN | Y-M: 20[redacted] | ONGOING |
| ZOLPIDEM | 10 mg | QD | Y-M: 20[redacted] | ONGOING |
| EZETIMIBE | 10 mg | QD | Y-M: 20[redacted] | ONGOING |
| MELOXICAM | 15 MG mg | QD | Y-M: 20[redacted] / -278 | ONGOING |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -259 | ONGOING |
| ATORVASTATIN | 40 mg | QD | Y-M: 20[redacted] / -132 | ONGOING |
| SODIUM CHLORIDE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] / 232 | Y-M: 20[redacted] / 232 |
| OSELTAMIVIR | 75 mg | BID | Y-M: 20[redacted] / 233 | Y-M: 20[redacted] / 242 |

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

**Event Description** INFLUENZA B
**Preferred term** インフルエンザ
**AE Onset Date / Rx Day** [redacted]20[redacted] / 233 (12 DAYS AFTER LAST TREATMENT)
**Age at AE Onset** 3[redacted]
**Laboratory Testing**

[redacted]20[redacted] (RX DAY 233): Basophils: 0.04 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.5 [0 - 2] %; Creatine Kinase: 173 [26 - 192] U/L; Creatinine: 49 [53 - 88] UMOL/L; Eosinophils: 0.08 [0.05 - 0.4] 10^9/L; Eosinophils/Leukocytes: 1 [1 - 4] %; Erythrocytes: 4.2 [4 - 5.3] 10^12/L; Glucose: 8.2 [3.9 - 5.5] MMOL/L; Hematocrit: 0.38 [0.36 - 0.48] FRACTION OF 1; Hemoglobin: 121 [120 - 160] G/L; Leukocytes: 8.2 [3.8 - 10.8] 10^9/L; Lymphocytes: 0.97 [0.96 - 4.32] 10^9/L; Lymphocytes/Leukocytes: 11.8 [20 - 44] %; Monocytes: 0.41 [0.27 - 0.82] 10^9/L; Monocytes/Leukocytes: 5 [2 - 9] %; NPTST275-FREE T4 THYROXINE: 1.1 [0.7 - 15] NG/DL; NPTST429-MCV: 90 [81 - 99] FL; NPTST432-MEAN CORPUSCULAR HEMOGLOBIN: 28.9 [27 - 33] PG; NPTST433-MEAN CORPUSCULAR HEMOGLOBIN CON: 32.2 [32 - 36] G/DL; NPTST441-META/MYELO/PRO: 1.0 [NOT REPORTED - 0.6] %; NPTST442-META/MYELO/PRO, ABSOLUTE: 0.08 [NOT REPORTED - 0.05] K/UL; NPTST454-MPV: 9.1 [9.4 - 12.4] FL; NPTST522-POCT BETA HCG: 5.0 [50 - NOT REPORTED] IU/L; NPTST566-RDWSD: 45.9 [35 - 46] FL; NPTST656-TSH WITH REFLEX FREE T4: 6.64 [0.35 - 4.94] IU/ML; Neutrophils/Leukocytes: 6.61 [50 - 70] %; Neutrophils/Leukocytes: 80.7 [50 - 70] %; Platelets: 261 [130 - 400] 10^9/L; Potassium: 3.1 [3.6 - 5] MMOL/L; Sodium: 135 [137 - 146] MMOL/L; [redacted]20[redacted] (RX DAY

234): Erythrocytes: 3.9 [4 - 5.3] 10^12/L; Hematocrit: 0.36 [0.36 - 0.48] FRACTION OF 1; Hemoglobin: 112 [120 - 160] G/L; Leukocytes: 5.8 [4 - 10.8] 10^9/L

**Microbiology**

[redacted]20[redacted] (RX DAY 233): OTHER NASOPHARYNX SWAB NPTST382-INFLUENZA A ANTIGENS RAPID: Negative; OTHER NASOPHARYNX SWAB NPTST386-INFLUENZA B ANTIGENS RAPID: Positive

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 233): CHEST PA & LATERAL X RAY: IMPRESSION NO ACUTE CARDIOPULMONARY FINDINGS. FINDINGS HEART SIZE AND VASCULARITY APPEAR NORMAL. LUNGS ARE CLEAR. COSTOPHRENIC ANGLES ARE SHARP. NO PNEUMOTHORAX. NO ACUTE OSSEOUS ABNORMALITY.; EKG: SINUS TACHYCARDIA, LEFT POSTERIOR FASCICULAR BLOCK, ABNORMAL ECG

| | |
|---|---|
| **AE Stopped Rx Day** | 235 (14 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 3 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

治験責任医師からの報告。本被験者は米国の 3[redacted] 歳女性であり，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，B 型インフルエンザの事象を発現した。

**Event 2 の臨床経過：**

関連する病歴は，乾癬性病変，1 型糖尿病，高コレステロール血症，洞性頻脈，関節症性乾癬，乾癬性関節炎，非喫煙者及び飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は B 型インフルエンザを発現した。20[redacted] 年 [redacted] 月 [redacted] 日，B 型インフルエンザは消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，CPK 値上昇の非重篤事象のため治験薬の投与が中止された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は頻脈となり救急診療科を受診した。心電図検査が行われ，洞性頻脈が認められた。被験者は 2 L の静脈内輸液を受けたが，心拍数は改善せず入院した。入院中にB型インフルエンザを合併し，タミフルを投与され，静脈内持続輸液を受けた。入院中，被験者のインスリンポンプは中止され，ランタス及びインスリン・スライディングスケールによる血糖コントロールが行われた。退院前日に被験者のインスリンポンプが再開され，血糖コントロールは良好であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者の心拍数に改善が認められたが，インフルエンザによると考えられる全身痛が持続した。被験者は経口摂取ができるようになり，同日退院した。

投与された薬剤は，タミフルであった。

**The patient's past medications include:**

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

TRIAMICINOLE for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Influenza B virus infection (10022003) (Influenza (10022000) ) [v.22.1] [10022003]

**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)

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Event of INFLUENZA B

**- Investigator:** Not applicable

**- AbbVie:** Event is common in the general population during the flu season.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] CHEST PA & LATERAL X RAY:** Impression no acute cardiopulmonary findings. Findings heart size and vascularity appear normal. Lungs are clear. Costophrenic angles are sharp. No pneumothorax. No acute osseous abnormality.

[redacted] **20[redacted] EKG:** Sinus tachycardia, left posterior fascicular block, abnormal ECG

[redacted] **20[redacted] INFLUENZA A ANTIGENS RAPID:** Negative

[redacted] **20[redacted] INFLUENZA B ANTIGENS RAPID:** Positive

[redacted] **20[redacted] POCT BETA HCG:** 5.0 IU/L

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 |
|---|---|---|---|---|
| 肝性脳症 | X | X | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| ADA 40 mg EOW | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| HEPATITIS: HEPATITIS C WITHOUT COMA,CHRONIC | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| HEPATITIS: CIRRHOSIS OF LIVER | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| OTHER: HYPERTROPHIC CARDIOMYOPTHY | 20[redacted] |
| GASTROESOPHAGEAL REFLUX DISEASE | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| Not reported. | |

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

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 172 | 172 |

**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] |
| FISH OIL | 1280 mg | QD | Y-M: 20[redacted] |
| NAPROXEN | 440 mg | QD | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20 |
| AMINO ACIDS NOS W/CAFFEINE/CITRUS AURANTIUM/G | 4 OTHER: TABLETS | QD | Y-M: 20 |
| ATENOLOL | 50 mg | QD | Y-M: 20 - |
| OMEPRAZOLE | 20 mg | PRN | Y-M: 20 - |
| TRIAMCINOLONE | 1 OTHER: APP | PRN | Y-M: 20 |
| FOLIC ACID | 1 mg | QD | Y-M: 20 - / -159 |
| METHOTREXATE | 12.5 mg | EVERY WEEK | Y-M: 20 - / -159 |
| METHOTREXATE | 12.5 mg | EVERY WEEK | Y-M: 20 - / -62 |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20 - / -55 |
| METHOTREXATE | 17.5 mg | EVERY WEEK | Y-M: 20 - / -48 |

**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 |
|---|---|---|---|---|
| FISH OIL | 1280 mg | QD | Y-M: 20 | Y-M: 20 - / 93 |
| NAPROXEN | 440 mg | QD | Y-M: 20 | Y-M: 20 - / 93 |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20 | Y-M: 20 - / 93 |
| AMINO ACIDS NOS W/CAFFEINE/CITRUS AURANTIUM/G | 4 OTHER: TABLETS | QD | Y-M: 20 | Y-M: 20 - / 93 |
| ATENOLOL | 50 mg | QD | Y-M: 20 - 12 | Y-M: 20 - / 93 |
| OMEPRAZOLE | 20 mg | PRN | Y-M: 20 - 02 | Y-M: 20 - / 93 |
| FOLIC ACID | 1 mg | QD | Y-M: 20 - / -159 | Y-M: 20 - / 93 |
| METHOTREXATE | 17.5 mg | EVERY WEEK | Y-M: 20 - / -48 | Y-M: 20 - / 88 |
| FOLINIC ACID | 5 mg | OTHER: 12HRS POST MTX AND 24 HOURS POST MTX | Y-M: 20 - / 39 | Y-M: 20 - / 89 |
| LACTULOSE | 20 mg | TID | Y-M: 20 - / 95 | Y-M: 20 - / 95 |
| ATENOLOL | 50 mg | QD | Y-M: 20 - / 98 | ONGOING |

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

| | |
|---|---|
| **Event Description** | HEPATIC ENCEPHALOPATHY |
| **Preferred term** | 肝性脳症 |
| **AE Onset Date / Rx Day** | 20 / 94 |
| **Age at AE Onset** | 5 |

**Laboratory Testing**

20 (RX DAY 94): Alanine Aminotransferase: 19 [0 - 40] U/L; Albumin: 40 [35 - 50] G/L; Alkaline Phosphatase: 84 [30 - 130] U/L; Aspartate Aminotransferase: INVALID -HEMOLYSIS [0 - 37] U/L; Bilirubin: 34 [0 - 21] UMOL/L; NPTST039-AMMONIA: 135 [0 - 72] UMOL/L; NPTST537-PROTHROMBIN TIME: 12.2 [9.3 - 11.7] SEC; Prothrombin Intl. Normalized Ratio: 1.21 [0.9 - 1.1] RATIO; 20 (RX DAY 95): NPTST351-HOMOCYSTEINE: 9.7 [0 - 12.2]

UMOL/L; [redacted]20[redacted] (RX DAY 113): NPTST039-AMMONIA: 141 [0 - 72] UMOL/L; NPTST693-VITAMIN B12: 591 [200 - 1100] (PG/MOL); [redacted]20[redacted] (RX DAY 120): NPTST039-AMMONIA: 118 [0 - 72] UMOL/L; [redacted]20[redacted] (RX DAY 148): NPTST039-AMMONIA: 139 [0 - 72] UMOL/L; [redacted]20[redacted] (RX DAY 171): NPTST039-AMMONIA: 132 [0 - 72] UMOL/L; [redacted]20[redacted] (RX DAY 182): NPTST039-AMMONIA: 96 [0 - 72] UMOL/L; [redacted]20[redacted] (RX DAY 196): NPTST039-AMMONIA: 97 [0 - 72] UMOL/L; NPTST692-VITAMIN B1 (THIAMINE): 12 [8 - 30] 099,NMOL/L

**Microbiology**

[redacted]20[redacted] (RX DAY 94): OTHER NASAL SWAB NPTST457-MRSA SURVEILLANCE CULTURE: Negative-NEGATIVE

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 94): CT HEAD/BRAIN WITHOUT CONTRAST: NORMAL UNENHANCED CRANIAL CT; MRA ARTERIOGRAM OF THE HEAD AND NECK WITH CONTRAST: NEGATIVE; MRI BRAIN WITH/WITHOUT CONTRAST: NEGATIVE; ULTRASOUND ABDOMEN COMPLETE: UNREMARKABLE SONOGRAM OF THE ABDOMEN; [redacted]20[redacted] (RX DAY 95): 2D ECHOCARDIOGRAM TRANSTHORACIC: LEFT VENTRICLE NORMAL IN SIZE AND SYSTOLIC FUNCTION; NO SIGNIFICANT VALVULAR ABNORMALITIES; DIASTOLIC FUNCTION IS NORMAL; NO EVIDENCE OF VEGETATION OR CARDIAC SOURCE OF EMBOLI; MILD LAE

| | |
|---|---|
| **AE Stopped Rx Day** | 254 (98 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 161 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，肝性脳症の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，C 型肝炎（慢性型，肝性昏睡なし），元喫煙者（1 日 1 箱を 20 年間），局面型乾癬，肝硬変，高血圧，肥大型心筋症，乾癬性関節炎及び元飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肝性脳症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肝性脳症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者より，前日の夜に「変な」感じがあったと報告された。被験者は，眠ることはできたものの寝過ごし，目覚まし時計の音も聞こえなかった。被験者は出勤したが，プリントしたり，パスワードを入力したりといった単純な作業ができなかった。同日，被験者は，錯乱，記憶障害及び不明瞭発語により，妻に連れられて救急治療室を受診した。被験者は，不明瞭発語，錯乱，そしてTIA又は薬剤の副作用の可能性のため，観察室に入院した。肝パネル検査の結果はビリルビン増加以外は正常で，神経症状と血清アンモニア値に基づき肝性脳症と診断された。血中アンモニアを低下させる目的でラクツロースが投与された。20[redacted] 年 [redacted] 月 [redacted] 日，腹部超音波検査で肝硬変やその他の急性病変は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は安定状態で退院した。被験者は意識清明で見当識障害はなく，途中で息継ぎをすることなく完全な文章で話すことができた。治験薬及びメトトレキサートの中止後に神経症状は改善したが，ベースラインの状態には戻っていなかった。

治験薬の投与が再開され，血清アンモニア値のモニタリングが行われた。20[redacted] 年 [redacted] 月 [redacted] 日，24 週後の規定来院時において，神経症状が悪化した。被験者によれば，精神的混濁は治験薬再開後に悪化した。

治験薬の投与は完全に中止された。

投与された薬剤はラクツロースであった。

**The patient's past medications include:**

TRIAMCINOLONE for PSORIASIS (20[redacted] - [redacted] 20[redacted])

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

Causality for UPADACITINIB (Blinded)

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1) Hepatic encephalopathy (10019660) (Hepatic encephalopathy (10019660) ) [v.23.0] [10019660]

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

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

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction recurred

Alternative Etiology for UPADACITINIB (Blinded)

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Event of HEPATIC ENCEPHALOPATHY

**- Investigator:** Not Applicable

**- AbbVie:** event is more likely related to pre-existing chronic hepatitis C and cirrhosis of liver.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] 2D ECHOCARDIOGRAM TRANSTHORACIC:** LEFT VENTRICLE NORMAL IN SIZE AND SYSTOLIC FUNCTION; NO SIGNIFICANT VALVULAR ABNORMALITIES; DIASTOLIC FUNCTION IS NORMAL; NO EVIDENCE OF VEGETATION OR CARDIAC SOURCE OF EMBOLI; MILD LAE.

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 19 U/L (normal 0 to 40)

[redacted] **20[redacted] ALBUMIN:** 3.7 G/L (normal 3.3 to 4.9)

[redacted] **20[redacted] ALBUMIN:** 4.1 G/L (normal 3.3 to 4.9)

[redacted] **20[redacted] ALBUMIN:** 4.0 G/DL (normal 3.5 to 5.0)

[redacted] **20[redacted] ALBUMIN:** 4.1 G/L (normal 3.3 to 4.9)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 84 U/L (normal 30 to 130)

[redacted] **20[redacted] AMMONIA:** 135 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 141 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 141 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 118 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 139 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 132 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 96 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 97 umol/L (normal 0 to 72)

[redacted] 20[redacted] **BILIRUBIN:** 2.0 mg/dL (normal 0.0 to 1.2)

[redacted] 20[redacted] **CT HEAD/BRAIN WITHOUT CONTRAST:** Normal unenhanced cranial CT.

[redacted] 20[redacted] **HOMOCYSTEINE:** 9.7 MMOL/L (normal 0 to 12.2)

[redacted] 20[redacted] **INTERNATIONAL NORMALIZED RATIO:** 1.21 ratio (normal 0.9 to 1.1)

20[redacted] **LIVER BIOPSY:** cirrhosis due to hepatitis C

[redacted] 20[redacted] **MRA ARTERIOGRAM OF THE HEAD AND NECK WITH CONTRAST:** Negative.

[redacted] 20[redacted] **MRI BRAIN WITH/WITHOUT CONTRAST:** Negative

[redacted] 20[redacted] **MRSA SURVEILLANCE CULTURE:** Negative

[redacted] 20[redacted] **PROTHROMBIN TIME:** 12.2 SEC (normal 9.3 to 11.7)

[redacted] 20[redacted] **SGOT:** 32 U/L (normal 11 to 36)

[redacted] 20[redacted] **SGOT:** 38 U/L (normal 11 to 36)

[redacted] 20[redacted] **SGOT:** 24 U/L (normal 11 to 36)

[redacted] 20[redacted] **SGPT:** 20 U/L (normal 6 to 43)

[redacted] 20[redacted] **SGPT:** 29 U/L (normal 6 to 43)

[redacted] 20[redacted] **SGPT:** 18 U/L (normal 6 to 43)

[redacted] 20[redacted] **ULTRASOUND ABDOMEN COMPLETE:** Unremarkable sonogram of the abdomen

[redacted] 20[redacted] **VITAMIN B1 (THIAMINE):** 12 nmol/L (normal 8 to 30)

[redacted] 20[redacted] **VITAMIN B12:** 591 pg/mol (normal 200 to 1100)

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 |
|---|---|---|---|---|
| 敗血症 | X | X | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 15 mg QD | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: AORTIC STENOSIS, CONGENITAL | 19[redacted] |
| VALVULAR HEART DISEASE: UNICUSPID VALVE | 19 |
| HEPATITIS: HEPATITIS C | 19 |
| VALVULAR HEART DISEASE: BICUSPID AORTIC VALVE REPAIR | 19 |
| VALVULAR HEART DISEASE: BICUSPID AORTIC VALVE REPAIR | 20 |
| VALVULAR HEART DISEASE: BICUSPID AORTIC VALVE REPLACEMENT | 20 |
| OTHER: ACTIVE PLAQUE PSORIASIS | 20 |
| PSORIATIC ARTHRITIS | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| Not reported. | |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 63 | 63 |

**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] |
| WARFARIN | 7 mg | QD | Y-M: 20[redacted] |
| VITAMINS NOS | 1 OTHER: TAB | QD | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| APREMILAST | 30 mg | BID | Y-M: 20[redacted] / -131 |
| PARACETAMOL | 625 mg | PRN | Y-M: 20[redacted] / -124 |

**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 |
| WARFARIN | 7 mg | QD | Y-M: 20[redacted] | ONGOING |
| VITAMINS NOS | 1 OTHER: TAB | QD | Y-M: 20[redacted] | ONGOING |
| APREMILAST | 30 mg | BID | Y-M: 20[redacted] / -131 | ONGOING |
| PARACETAMOL | 625 mg | PRN | Y-M: 20[redacted] / -124 | ONGOING |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 55 | Y-M: 20[redacted] / 64 |
| CARVEDILOL | 6.25 mg | BID | Y-M: 20[redacted] / 77 | ONGOING |
| LISINOPRIL | 5 mg | QD | Y-M: 20[redacted] / 77 | ONGOING |
| PARACETAMOL | 975 mg | PRN | Y-M: 20[redacted] / 77 | ONGOING |
| SODIUM CHLORIDE | 10 mL | OTHER: AS DIRECTED | Y-M: 20[redacted] / 77 | ONGOING |
| SODIUM CHLORIDE | 3 L | OTHER: ONCE | Y-M: 20[redacted] / 77 | Y-M: 20[redacted] / 77 |
| CEFEPIME | NOT REPORTED | OTHER: UNK | Y-M: 20[redacted] / 77 | Y-M: 20[redacted] / 79 |
| DOXYCYCLINE | NOT REPORTED | OTHER: UNK | Y-M: 20[redacted] / 77 | Y-M: 20[redacted] / 79 |
| VANCOMYCIN | NOT REPORTED | OTHER: UNK | Y-M: 20[redacted] / 77 | Y-M: 20[redacted] / 79 |
| HEPARIN | NOT REPORTED | OTHER: UNK | Y-M: 20[redacted] / 77 | Y-M: 20[redacted] / 84 |
| CEFTRIAXONE | 2 g | QD | Y-M: 20[redacted] / 79 | ONGOING |
| GENTAMICIN | 100MG/50ML-NACL 0.9% mg | QD | Y-M: 20[redacted] / 79 | ONGOING |
| DICLOFENAC | 1.3 % | PRN | Y-M: 20[redacted] / 84 | ONGOING |
| METHOCARBAMOL | 750 mg | PRN | Y-M: 20[redacted] / 84 | ONGOING |

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

| | |
|---|---|
| **Event Description** | ACUTE SEPSIS |
| **Preferred term** | 敗血症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 55 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 77): Glucose: 7.2 [4.1 - 5.9] MMOL/L; Leukocytes: NORMAL [NOT REPORTED - NOT REPORTED] UNK; NPTST559-RAPID TROPONIN: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT

REPORTED; NPTST664-URINALYSIS: UNREMARKABLE [NOT REPORTED - NOT REPORTED] NA; [redacted]20[redacted] (RX DAY 82): NPTST653-TROUGH AND PEAK LEVEL FOR GENTA: UNK [NOT REPORTED - NOT REPORTED] UNK; [redacted]20[redacted] (RX DAY 84): Prothrombin Intl. Normalized Ratio: 3.39 [0.8 - 1.1] RATIO

**Microbiology**

[redacted]20[redacted] (RX DAY 77): BLOOD NPTST211-CULTURE: Positive-GRAM-POSITIVE COCCI BACTEREMIA

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 77): ECHOCARDIOGRAM: MODERATE TO SEVERE EF (30-35%);DID NOT REVEAL PRESENCE OF VEGETATION; EKG: SINUS TACHYCARDIA, CHRONIC LEFT BUNDLE BRANCH BLOCK; [redacted]20[redacted] (RX DAY 79): TRANSESOPHAGEAL ECHOCARDIOGRAM: LEFT VENTRICLE: THE CAVITY SIZE INCREASED. SYSTOLIC FUNCTION IS MODERATELY TO SEVERELY REDUCED. THE ESTIMATED EJECTION FRACTION IS 35%.TRICUSPID VALVE: MILD REGURGITATION.

| | |
|---|---|
| **AE Stopped Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

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，急性敗血症の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，大動脈狭窄（先天性），大動脈一尖弁，大動脈二尖弁置換，C 型肝炎，人工心臓弁を用いた大動脈弁置換術，活動性局面型乾癬，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性敗血症を発現した。

被験者は 11 歳時に先天性大動脈二尖弁修復術を受けていたが，大動脈狭窄が進行した。20[redacted] 年，被験者は人工心臓弁置換術を受けた。20[redacted] 年 [redacted] 月，駆出率が 55%であった。

入院前において，被験者の症状は船旅に出る直前の 20[redacted] 年 [redacted] 月 [redacted] 日に出現した。20[redacted] 年 [redacted] 月 [redacted] 日，治験薬の投与が完全に中止された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，約 3 週間続いている一過性の発熱（104°F）のため ER を受診した。発熱は船旅の 2 日目に出現した。そのほかにも被験者は，悪心，空吐き（嘔吐なし）を伴う食欲喪失，胸部上部不快感及び発熱に伴う寝汗を訴えた。ER で行われた心電図検査で，洞性頻脈及び虚血性変化を伴わない慢性左脚ブロックが認められた。心内膜炎の可能性が疑われた。同日，被験者は入院した。心エコー検査で中等度から重度の駆出率（30%～35%）が認められた。経胸壁心エコー検査及び経食道心エコー検査で大動脈弁疣贅は認められなかったが，血液培養で緑色連鎖球菌が認められた。このような状況において，来院時の推定される人工大動脈弁心内膜炎，先行して行われた歯科治療，既存の人工心臓弁，及び血液培養で特定された病原菌に対する治療が行われた。まず，バンコマイシン，セフェピム及びドキシサイクリンの投与が開始された。血液培養の結果が得られると，セフトリアキソン及びゲンタマイシンの静脈内投与に切り替えられた。20[redacted] 年 [redacted] 月 [redacted] 日，PICC ライン留置術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者の状態は問題なく，退院した。退院時までに行われた抗生物質療法の期間は計 5 週間であった。

投与された薬剤は，ゲンタマイシン，塩化ナトリウム，リシノプリル，ヘパリン，セフトリアキソン，ドキシサイクリン，タイレノール，バンコマイシン及びセフェピムであった。

Causality for ABT-494 (Blinded)

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1) Sepsis (10040047) (Sepsis (10040047) ) [v.22.0] [10040047]

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

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

**Dechallenge:** No

Alternative Etiology for ABT-494 (Blinded)

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Event of ACUTE SEPSIS

**- Investigator:** Not applicable

**- AbbVie:** Not applicable

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] BLOOD CULTURE:** Positive (Streptococcus viridans)

**Unknown date BODY TEMPERATURE:** 104 F

**20[redacted] CARDIAC CATHETERIZATION:** Normal

[redacted] **20[redacted] ECHOCARDIOGRAM:** Left Ventricle: Moderate to severe reduced EF (30-35%) Aortalve: Mechanical prosthetic valve Mitral Valve: Mild regurgitation Aortic Root: Poorly visualized, moderately dilated

[redacted] **20[redacted] EJECTION FRACTION:** 55%

[redacted] **20[redacted] VITALS:** Discharge vitals: T 36.5C; Tmin 36.3C; Tmax 36.9; HR 72(monitored), RR 18; BP 119/77; SpO2 98%

[redacted] **20[redacted] EKG:** Sinus tachycardia, chronic left bundle branch block

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Occasional supraventricular premature complex, left bundle branch block.

[redacted] **20[redacted] GLUCOSE:** 129

**Unknown date HEMOGLOBIN:** Normal

[redacted] **20[redacted] INTERNATIONAL NORMALIZED RATIO:** 3.39

**Unknown date LACTIC ACID:** 2.8 no unit

**Unknown date PLATELETS:** Normal

[redacted] **20[redacted] TRANSESOPHAGEAL ECHOCARDIOGRAM:** Aortic Valve: No obvious vegetations Mitral Valve: Leaflets are mildly thickened, Mild regurgitation, minute mobile echodensities likely benign fibrinous strands Left ventricle: The cavity size increased. Systolic function is moderately to severely reduced. The estimated ejection fraction is 35%.tricuspid valve: Mild regurgitation. Aorta: ascending aorta is moderately dilated, no atheroma

[redacted] **20[redacted] TROPONIN:** Rapid-negative

[redacted] **20[redacted] URINALYSIS:** Unremarkable

**Unknown date WHITE BLOOD CELLS:** Normal

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 |
|---|---|---|---|
| ADA 40 mg EOW | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| HYPOTHYROIDISM | 19[redacted] |
| OTHER: MOTORCYCLE ACCIDENT | 19 |
| OTHER: OVARIAN CYSTS | 19 |
| OSTEOARTHRITIS | 20 |
| OTHER: CERVICAL DISC DISORDER | 20 |
| OTHER: CERVICAL RADICULOPATHY | 20 |
| OTHER: COMPOUND FRACTURE RIGHT SHOULDER | 20 |
| OTHER: FALL | 20 |
| OTHER: CARPAL TUNNEL SYNDROME | 20 |
| OTHER: HYPERURICEMIA | 20 |
| OTHER: FRACTURED LEFT WRIST | 20 |
| OTHER: MOTOR VEHICLE ACCIDENT | 20 |
| OTHER: ROTATOR CUFF TEAR LEFT SHOULDER | 20 |
| OTHER: PLAQUE PSORIASIS | 20 |
| PSORIATIC ARTHRITIS | 20 |
| HYPERLIPIDEMIA | 20 |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: HYSTERECTOMY | 19[redacted] |
| SURGERY: BREAST REDUCTION | 19 |
| SURGERY: SURGICAL REPAIR OF COMPOUND FRACTURE OF RIGHT SHOULDER | 20 |
| SURGERY: RIGHT CARPAL TUNNEL RELEASE | 20 |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 166 | 166 |
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 167 | [redacted]20[redacted] / 391 | 225 |
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 392 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| LEVOTHYROXINE | 175 OTHER: MCG | QD | Y-M: 19[redacted] |
| TRAMADOL | 50 mg | QD | Y-M: 20[redacted] |
| HEPATITIS B IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| PREGABALIN | 50 mg | QD | Y-M: 20[redacted] |
| ALLOPURINOL | 100 mg | BID | Y-M: 20[redacted] / -363 |
| DULOXETINE | 60 mg | QD | Y-M: 20[redacted] / -210 |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -100 |
| METHOTREXATE | 10 mg | EVERY WEEK | Y-M: 20[redacted] / -100 |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] / -59 |
| SIMVASTATIN | 10 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-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| LEVOTHYROXINE | 175 OTHER: MCG | QD | Y-M: 19[redacted] | NOT REPORTED |
| TRAMADOL | 50 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 356 |
| PREGABALIN | 50 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| DULOXETINE | 60 mg | QD | Y-M: 20[redacted] / -210 | NOT REPORTED |
| FOLIC ACID | 1 mg | QD | Y-M: 20[redacted] / -100 | NOT REPORTED |
| METHOTREXATE | 10 mg | EVERY WEEK | Y-M: 20[redacted] / -100 | NOT REPORTED |
| SIMVASTATIN | 10 mg | QD | Y-M: 20[redacted] / -57 | NOT REPORTED |
| ASCORBIC ACID | 1000 mg | QD | Y-M: 20[redacted] / 186 | NOT REPORTED |
| ATORVASTATIN | 40 mg | QD | Y-M: 20[redacted] / 237 | NOT REPORTED |
| METFORMIN | 1000 mg | BID | Y-M: 20[redacted] / 237 | NOT REPORTED |
| PREDNISONE | 2.5 mg | QD | Y-M: 20[redacted] / 308 | Y-M: 20[redacted] / 356 |
| ACETYLSALICYLIC ACID | 81 mg | BID | Y-M: 20[redacted] / 356 | NOT REPORTED |
| KETOROLAC | 10 mg | PRN | Y-M: 20[redacted] / 356 | Y-M: 20[redacted] / 358 |
| VICODIN | 7.5 mg | PRN | Y-M: 20[redacted] / 356 | Y-M: 20[redacted] / 366 |
| CELECOXIB | 200 mg | QD | Y-M: 20[redacted] / 359 | Y-M: 20[redacted] / 373 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING OF OSTEOARTHRITIS OF LEFT KNEE |
| **Preferred term** | 変形性関節症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 343 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 356): Glucose: 5.3 [3.3 - 8.3] MMOL/L; [redacted]20[redacted] (RX DAY 357): Blood Urea Nitrogen: 4.3 [2.5 - 6.4] MMOL/L; Calcium: 2.07 [2.12 - 2.52] MMOL/L; Chloride: 105 [98 - 107] MMOL/L; Creatinine: 80 [49 - 90] UMOL/L; Erythrocytes: 3.6 [4.2 - 5.4] 10^12/L; Glucose: 6.6 [3.9 - 6.1] MMOL/L; Glucose: 7.4 [3.3 - 8.3] MMOL/L; Hematocrit: 0.34 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 112 [120 - 150] G/L; Leukocytes: 12 [4.1 - 10.2] 10^9/L; NPTST044-ANION GAP: 8 [3 - 15] MMOL/L; NPTST176-CO2: 27 [21 - 32] MMOL/L; Platelets: 230 [130 - 400] 10^9/L; Potassium: 4.9 [3.5 - 5.1] MMOL/L; Sodium: 138 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 358): Blood Urea Nitrogen: 6.1 [2.5 - 6.4] MMOL/L; Calcium: 2.05 [2.12 - 2.52] MMOL/L; Chloride: 106 [98 - 107] MMOL/L; Creatinine: 71 [49 - 90] UMOL/L; Erythrocytes: 3.5 [4.2 - 5.4] 10^12/L; Glucose: 6.3 [3.9 - 6.1] MMOL/L; Hematocrit: 0.33 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 105 [120 - 150] G/L; Leukocytes: 10.7 [4.1 - 10.2] 10^9/L; NPTST044-ANION GAP: 6 [3 - 15] MMOL/L; NPTST176-CO2: 30 [21 - 32] MMOL/L; Platelets: 228 [130 - 400] 10^9/L; Potassium: 4.4 [3.5 - 5.1] MMOL/L; Sodium: 140 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 359): Blood Urea Nitrogen: 4.3 [2.5 - 6.4] MMOL/L; Calcium: 2.17 [2.12 - 2.52] MMOL/L; Chloride: 110 [98 - 107] MMOL/L; Creatinine: 53 [49 - 90] UMOL/L; Erythrocytes: 3.6 [4.2 - 5.4] 10^12/L; Glucose: 5.2 [3.9 - 6.1] MMOL/L; Hematocrit: 0.33 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 107 [120 - 150] G/L; Leukocytes: 7.9 [4.1 - 10.2] 10^9/L; NPTST176-CO2: 30 [21 - 32] MMOL/L; Platelets: 211 [130 - 400] 10^9/L; Potassium: 4.3 [3.5 - 5.1] MMOL/L; Sodium: 144 [136 - 145] MMOL/L

**Microbiology**

NOT REPORTED

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 356): TOTAL LEFT KNEE REPLACEMENT: SUCCESSFUL TOTAL LEFT KNEE REPLACEMENT WITH NO COMPLICATIONS; [redacted]20[redacted] (RX DAY 359): LEFT TOTAL KNEE XRAY: WELL POSITIONED LEFT TOTAL KNEE IMPLANT IN APPROPRIATE POSITION AND ALIGNMENT

| | |
|---|---|
| **AE Stopped Rx Day** | 359 |
| **Duration of AE** | 17 DAYS |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | DISEASE PROGRESSION |
| **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:** M15-572

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，左膝の変形性関節症の悪化の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，甲状腺機能低下症，オートバイ事故，子宮摘出，転倒，変形性関節症，高尿酸血症，自動車事故，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。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左膝の変形性関節症の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左膝の変形性関節症の悪化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左膝の疼痛悪化及び可動制限のため整形外科医を受診した。整形外科医は，左膝の人工膝関節全置換術が必要と判断した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，人工膝関節全置換術を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for UPADACITINIB (Blinded)

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1) Osteoarthritis aggravated (10031162) (Osteoarthritis (10031161) ) [v.23.0] [10031162]

**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 WORSENING OF OSTEOARTHRITIS OF LEFT KNEE

**- Investigator:** Disease progression

**- AbbVie:** Event is more likely related to pre-existing osteoarthritis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] COVID-19 BLOOD TEST:** Negative

[redacted] **20[redacted] HEMATOCRIT:** 33.4 % (normal 37.0 to 47.0)

[redacted] **20[redacted] HEMOGLOBIN:** 10.7 G/DL (normal 12.0 to 15.0)

[redacted] **20[redacted] KNEE X-RAY:** Well positioned left total knee implant in appropriate position and alignment

[redacted] **20[redacted] PLATELET COUNT:** 211 10^3/ul (normal 130 to 400)

[redacted] **20[redacted] WBC:** 11.98 10^3/ul (normal 4.10 to 10.20)

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 |
|---|---|---|---|
| UPA 30 mg QD | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: PLAQUE PSORIASIS | 19[redacted] |
| OSTEOARTHRITIS: BILATERAL KNEES | 20[redacted] |
| OTHER: BILATERAL ACHILLES TENDINITIS | 20[redacted] |
| KIDNEY DISORDER: KIDNEY STONES | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: REMOVAL OF KIDNEY STONES | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 20 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 181 | 181 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 182 | [redacted]20[redacted] / 393 | 212 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 394 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| METHOTREXATE | 10 mg | EVERY WEEK | Y-M: 20[redacted] / -116 |
| TRIAMCINOLONE | 0.5 % | TID | Y-M: 20[redacted] / -116 |
| METHOTREXATE | 5 mg | EVERY WEEK | Y-M: 20[redacted] / -92 |
| TRAMADOL | 50 mg | BID | Y-M: 20[redacted] / -35 |

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

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| TRAMADOL | 50 mg | BID | Y-M: 20[redacted] / -35 | NOT REPORTED |
| CELECOXIB | 200 mg | PRN | Y-M: 20[redacted] / 291 | NOT REPORTED |
| ORPHENISAL | 50-770-60 mg | PRN | Y-M: 20[redacted] / 292 | Y-M: 20[redacted] / 393 |
| OXYCOCET | 5/325 mg | PRN | Y-M: 20[redacted] / 292 | Y-M: 20[redacted] / 393 |
| PREGABALIN | 50 mg | PRN | Y-M: 20[redacted] / 292 | Y-M: 20[redacted] / 393 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING OF OSTEOARTHRITIS |
| **Preferred term** | 変形性関節症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 139 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**
NOT REPORTED
**Microbiology**
NOT REPORTED
**SAE Supplemental Procedure**
[redacted]20[redacted] (RX DAY 291): LEFT TOTAL KNEE REPLACEMENT: SUCCESSFUL LEFT TOTAL KNEE REPLACEMENT SURGERY

| | |
|---|---|
| **AE Stopped Rx Day** | 298 |
| **Duration of AE** | 160 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | 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:** M15-572

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，変形性関節症の悪化の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，局面型乾癬，元喫煙者（1 日 1 箱を 20 年間），変形性関節症及び乾癬性関節炎であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は変形性関節症の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，変形性関節症の悪化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は変形性関節症による疼痛悪化のため入院し，待期的に左膝の人工膝関節全置換術を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

**The patient's past medications include:**

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

TRIAMCINOLONE for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Osteoarthritis aggravated (10031162) (Osteoarthritis (10031161) ) [v.23.0] [10031162]

**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 WORSENING OF OSTEOARTHRITIS

**- Investigator:** Osteoarthritis.

**- AbbVie:** Event is more likely related to pre-existing osteoarthritis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BODY WEIGHT:** 239.6 Pounds

[redacted] **20[redacted] BODY WEIGHT:** 242.2 Pounds

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 |
|---|---|---|---|---|
| 睡眠時無呼吸症候群 | X | | | |
| 創離開 | X | | | |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| ADA 40 mg EOW | 4[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: BELL PARALYSIS | 19[redacted] |
| PSORIATIC ARTHRITIS | 19[redacted] |
| OTHER: BELL PARALYSIS | 20[redacted] |
| OTHER: BILATERAL PLANTAR PSORIASIS PLAQUE | 20[redacted] |
| OTHER: NAIL PSORIASIS ON TOES | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| OTHER: SEROTONIN LEVEL DISORDER | 20[redacted] |
| OTHER: FIRST TOE DACTYLITIS | 20[redacted] |
| OTHER: SYNOVITIS LEFT WRIST , MCP | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: VASECTOMY | 20[redacted] |
| SURGERY: CHOLECYSTECTOMY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 8 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | More than 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 169 | 169 |
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 170 | [redacted]20[redacted] / 399 | 230 |
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 400 | [redacted]20[redacted] / 645 | 246 |

**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] |
| METHOTREXATE | 25 mg | EVERY WEEK | Y-M: 20[redacted] |
| DILTIAZEM | 240 mg | QD | Y-M: 20[redacted] / -217 |
| CITALOPRAM | 10 mg | QD | Y-M: 20[redacted] / -158 |

**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 |
|---|---|---|---|---|
| METHOTREXATE | 25 mg | EVERY WEEK | Y-M: 20[redacted] | NOT REPORTED |
| DILTIAZEM | 240 mg | QD | Y-M: 20[redacted] / -217 | NOT REPORTED |
| CITALOPRAM | 10 mg | QD | Y-M: 20[redacted] / -158 | NOT REPORTED |
| FOLIC ACID | 5 mg | EVERY WEEK | Y-M: 20[redacted] / 2 | NOT REPORTED |
| ALL OTHER NON-THERAPEUTIC PRODUCTS | NA | OTHER: FACIAL MASK | Y-M: 20[redacted] / 197 | NOT REPORTED |
| MOMETASONE | 2 OTHER: VAPORISATIONS | BID | Y-M: 20[redacted] / 301 | ONGOING |
| TRIAMCINOLONE | 20 mg | OTHER: ONLY ONCE | Y-M: 20[redacted] / 346 | Y-M: 20[redacted] / 346 |
| DEXAMETHASONE | 6 mg | OTHER: ONCE | Y-M: 20[redacted] / 366 | Y-M: 20[redacted] / 366 |
| HYDROMORPHONE | 0.5 mg | PRN | Y-M: 20[redacted] / 366 | Y-M: 20[redacted] / 367 |
| HYDROMORPHONE | 1 mg | PRN | Y-M: 20[redacted] / 366 | Y-M: 20[redacted] / 368 |
| PARACETAMOL | 1000 mg | PRN | Y-M: 20[redacted] / 366 | Y-M: 20[redacted] / 375 |
| LABETALOL | 10 mg | OTHER: ONCE | Y-M: 20[redacted] / 367 | Y-M: 20[redacted] / 367 |
| DEXAMETHASONE | 6 mg | OTHER: ONCE | Y-M: 20[redacted] / 370 | Y-M: 20[redacted] / 370 |
| GRANISETRON | 1 mg | OTHER: ONCE | Y-M: 20[redacted] / 370 | Y-M: 20[redacted] / 370 |
| HYDROMORPHONE | 0.5 mg | PRN | Y-M: 20[redacted] / 370 | Y-M: 20[redacted] / 370 |
| LABETALOL | 10 mg | OTHER: ONCE | Y-M: 20[redacted] / 370 | Y-M: 20[redacted] / 370 |
| DEXAMETHASONE | 6 mg | BID | Y-M: 20[redacted] / 370 | Y-M: 20[redacted] / 372 |
| TRIAMCINOLONE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 508 | Y-M: 20[redacted] / 508 |
| TRIAMCINOLONE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 647 | Y-M: 20[redacted] / 647 |

| | | | | |
|---|---|---|---|---|
| TRIAMCINOLONE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 728 | Y-M: 20[redacted] / 758 |
| AUGMENTIN | 875 mg | BID | Y-M: 20[redacted] / 811 | Y-M: 20[redacted] / 821 |
| TRIAMCINOLONE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 864 | Y-M: 20[redacted] / 864 |
| TRIAMCINOLONE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] / 929 | Y-M: 20[redacted] / 929 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | OBSTRUCTIVE SLEEP APNEA |
| **Preferred term** | 睡眠時無呼吸症候群 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 183 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **SAE Supplemental Procedure** | |
| [redacted]20[redacted] (RX DAY 366): BILATERAL LOWERING OF LOWER TURBINATES: RECOVERED; BILATERAL TONSILECTOMY: RECOVERED; SEPTOPLASTIA: RECOVERED; UVULO-PALATO PHARNGOPLASTY: RECOVERED | |
| **AE Stopped Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | RESPIRATORY TRACT ANATOMIC ABNORMALITIES |
| **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** | SURGICAL WOUND OPENING |
| **Preferred term** | 創離開 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 369 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **SAE Supplemental Procedure** | |
| [redacted]20[redacted] (RX DAY 369): LEFT TONSIL HEMOSTASIS REVISION BY CAUTERIZATION: WENT WELL , PATIENT DISCHARGE ON [redacted]. | |
| **AE Stopped Rx Day** | 369 |
| **Duration of AE** | 1 DAY |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |

| | |
|---|---|
| **Investigator Alternative Etiology** | SURGICAL INTERVENTION FOR OBSTRUCTIVE SLEEP APNEA |
| **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:** M15-572

治験責任医師からの報告。本被験者はカナダの 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，閉塞性睡眠時無呼吸及び手術創の開口の事象を発現した。

**Event 1 及び 2 の臨床経過：**

関連する病歴は，乾癬性関節炎，元喫煙者（1 日 1 箱を 8 年間），高血圧及び元飲酒者（1 日 4 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は閉塞性睡眠時無呼吸を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は手術創の開口を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，手術創の開口は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は閉塞性睡眠時無呼吸と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は睡眠時にマスクを使用する持続的気道陽圧法（CPAP）を開始した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は閉塞性睡眠時無呼吸に対する外科的処置のため入院し，同日手術が行われた。これらの手術は，鼻中隔形成術，両側下鼻甲介切除術，両側扁桃摘出術及び口蓋垂口蓋咽頭形成術であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は手術創の開口により再入院した。喉に出血が見られ，再入院を指示された。創傷開口を閉鎖するための手術が行われ，焼灼で左扁桃が止血された。手術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，dilaudid，デカドロン及びタイレノールであった。

Causality for UPADACITINIB (Blinded)

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1) Obstructive sleep apnea syndrome (10055577) (Sleep apnoea syndrome (10040979) ) [v.22.1] [10055577]

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

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

**Dechallenge:** No

2) Wound dehiscence (10048031) (Wound dehiscence (10048031) ) [v.22.1] [10048031]

**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)

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Event of OBSTRUCTIVE SLEEP APNEA

**- Investigator:** Respiratory tract anatomic abnormalities

**- AbbVie:** Etiology of the event is not consistent with the study drug's mechanism of action. Additional risk factors include male gender and subject is overweight.

Event of SURGICAL WOUND OPENING

**- Investigator: Surgical intervention for obstructive sleep apnea.**

**- AbbVie:** Event is more likely a complication related to surgical procedure done on [redacted] 20[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 |
|---|---|---|---|---|
| 帯状疱疹 | X | | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| UPA 15 mg QD | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: PSORIASIS | 19[redacted] |
| OTHER: PSORIASIS PLAQUE | 19[redacted] |
| OTHER: SEASONAL ALLERGY | 19[redacted] |
| OTHER: OCCASIONNAL DIARRHEA | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: VASECTOMY | 20[redacted] |

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

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 175 | 175 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 176 | [redacted]20[redacted] / 390 | 215 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 391 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| NISITA | 1 OTHER: APPLICATION | PRN | Y-M: 20[redacted] |
| MOMETASONE | 0.1 % | PRN | Y-M: 20[redacted] |
| ERGOCALCIFEROL | 10000 OTHER: UNITS | QD | Y-M: 20[redacted] / -172 |
| FISH OIL | 1 OTHER: TAB | OTHER: 3 TIMES WEEKS | Y-M: 20[redacted] / -172 |
| FOLIC ACID | 5 mg | OTHER: 6 DAYS OVER 7 | Y-M: 20[redacted] / -172 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -172 |
| VARICELLA ZOSTER VACCINE | 0.5 mL | OTHER: ONCE | Y-M: 20[redacted] / -146 |
| IBUPROFEN | 400 mg | BID | Y-M: 20[redacted] / -142 |
| HEPATITIS B IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] / -105 |
| HERPES ZOSTER IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] / -14 |
| VARICELLA ZOSTER VACCINE | 0.5 mL | OTHER: ONCE | Y-M: 20[redacted] / -14 |

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

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| NISITA | 1 OTHER: APPLICATION | PRN | Y-M: 20[redacted] | NOT REPORTED |
| ERGOCALCIFEROL | 10000 OTHER: UNITS | QD | Y-M: 20[redacted] / -172 | NOT REPORTED |
| FISH OIL | 1 OTHER: TAB | OTHER: 3 TIMES WEEKS | Y-M: 20[redacted] / -172 | NOT REPORTED |
| FOLIC ACID | 5 mg | OTHER: 6 DAYS OVER 7 | Y-M: 20[redacted] / -172 | NOT REPORTED |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / -172 | Y-M: 20[redacted] / 255 |
| IBUPROFEN | 400 mg | BID | Y-M: 20[redacted] / -142 | NOT REPORTED |
| HYDROCORTISONE | 1 % | PRN | Y-M: 20[redacted] / 15 | NOT REPORTED |
| ACICLOVIR | 1000 mg | TID | Y-M: 20[redacted] / 250 | Y-M: 20[redacted] / 257 |
| PREGABALIN | 50 mg | BID | Y-M: 20[redacted] / 253 | NOT REPORTED |
| ACICLOVIR | 800 mg | TID | Y-M: 20[redacted] / 257 | Y-M: 20[redacted] / 263 |
| METHOTREXATE | 20 mg | EVERY WEEK | Y-M: 20[redacted] / 273 | NOT REPORTED |

**Event #2: Serious Adverse Event, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | WORSENING OF HERPES ZOSTER |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 257 |
| **Age at AE Onset** | 5[redacted] |

| | |
|---|---|
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **SAE Supplemental Procedure** | |
| NOT REPORTED | |
| **AE Stopped Rx Day** | 285 |
| **Duration of AE** | 29 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | REQUIRES OR PROLONGS HOSPITALIZATION |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

治験責任医師からの報告。本被験者はカナダの 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，帯状疱疹の悪化の事象を発現した。

**Event 2 の臨床経過：**

関連する病歴は，乾癬，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。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹の悪化は消失した。

本事象発現前，20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹（非重篤）が出現した。20[redacted] 年 [redacted] 月 [redacted] 日，アシクロビルの投与が開始されたが，改善は見られず，新たな病変が認められた。この時点で治験薬の投与が休止された。

被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に救急治療室に紹介され，入院した。病歴及び身体的診察の結果に基づき，帯状疱疹と診断された。帯状疱疹は L1 及び T12 領域の右側の 2 つの皮膚分節に認めら

れた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者は 20[redacted] 年 [redacted] 月と 20[redacted] 年 [redacted] 月に帯状疱疹ワクチンを受けていた。水疱瘡及び帯状疱疹の病歴はなかった。

投与された薬剤は，リリカ及びアシクロビルであった。

**The patient's past medications include:**

ELOCOM for PSORIASIS (20[redacted] - [redacted] 20[redacted])

SHINGRIX for HERPES ZOSTER PREVENTION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster (10019974) (Herpes zoster (10019974) ) [v.22.1] [10019974]

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

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

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of WORSENING OF HERPES ZOSTER

**- Investigator:** Not applicabe

**- 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 |
|---|---|---|---|---|
| 基底細胞癌 | X | | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| Placebo to UPA 15 mg QD | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: TENDON INJURY (LEFT HAND, 1ST DIGIT) | 19[redacted] |
| OTHER: PLAQUE PSORIASIS | 19[redacted] |
| HYPERTENSION | 19[redacted] |
| OTHER: HYPERLIPIDEMIA | 19[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: ATRIAL FIBRULATION | 20[redacted] |
| OTHER: CEREBROVASCULAR ACCIDENT | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: LEFT 1ST TENDON SURGERY DUE TO INJURY | 19[redacted] |

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

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | 2 - 4 DRINKS |

**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] / 166 | 166 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 167 | [redacted]20[redacted] / 399 | 233 |
| ABT-494 | 15 MG | ORAL | QD | [redacted]20[redacted] / 400 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| DESONIDE | 0.05 % | PRN | Y-M: 19[redacted] |
| ASCORBIC ACID | 500 mg | QD | Y-M: 20[redacted] |
| CALCIUM | 650 mg | QD | Y-M: 20[redacted] |
| ERGOCALCIFEROL | 2000 IU | QD | Y-M: 20[redacted] |
| FISH OIL | 1 OTHER: TAB | QD | Y-M: 20[redacted] |
| SILYBUM MARIANUM | 2 OTHER: TABS | QD | Y-M: 20[redacted] |
| TOCOPHEROL | 400 IU | QD | Y-M: 20[redacted] |
| VITAMINS NOS | 1 OTHER: TAB | QD | Y-M: 20[redacted] |
| METHOTREXATE | 12.5 mg | EVERY WEEK | Y-M: 20[redacted] |
| CLOBETASOL | 0.05 % | PRN | Y-M: 20[redacted] |
| METOPROLOL | 25 mg | QD | Y-M: 20[redacted] |
| RIVAROXABAN | 20 mg | QD | Y-M: 20[redacted] |
| ROSUVASTATIN | 20 mg | QD | Y-M: 20[redacted] |
| PERINDOPRIL | 4 mg | QD | Y-M: 20[redacted] |
| DAIVOBET | 50 OTHER: MCG | PRN | Y-M: 20[redacted] / -314 |
| AMLODIPINE | 2.5 mg | QD | Y-M: 20[redacted] / -100 |

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

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| ASCORBIC ACID | 500 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| CALCIUM | 650 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| ERGOCALCIFEROL | 2000 IU | QD | Y-M: 20[redacted] | NOT REPORTED |
| SILYBUM MARIANUM | 2 OTHER: TABS | QD | Y-M: 20[redacted] | NOT REPORTED |
| TOCOPHEROL | 400 IU | QD | Y-M: 20[redacted] | NOT REPORTED |
| VITAMINS NOS | 1 OTHER: TAB | QD | Y-M: 20[redacted] | NOT REPORTED |
| METOPROLOL | 25 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| RIVAROXABAN | 20 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| ROSUVASTATIN | 20 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| PERINDOPRIL | 4 mg | QD | Y-M: 20[redacted] | NOT REPORTED |
| AMLODIPINE | 2.5 mg | QD | Y-M: 20[redacted] / -100 | NOT REPORTED |
| OTHER COMBINATIONS OF NUTRIENTS | 2 OTHER: CAPS | QD | Y-M: 20[redacted] / 113 | NOT REPORTED |
| LEFLUNOMIDE | 10 mg | QD | Y-M: 20[redacted] / 136 | ONGOING |
| CURCUMIN | 2 OTHER: CAPS | QD | Y-M: 20[redacted] / 240 | NOT REPORTED |
| TAMSULOSIN | 0.4 mg | QD | Y-M: 20[redacted] / 349 | NOT REPORTED |

**Event #1: Serious Adverse Event, Event of Interest - Possible Malignancy, Event of Interest - Malignancy, Event of Interest - Non-Melanoma Skin Cancer (NMSC)**

| | |
|---|---|
| **Event Description** | BASAL CELL CARCINOMA OF THE SKIN |
| **Preferred term** | 基底細胞癌 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 399 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **SAE Supplemental Procedure** | |
| NOT REPORTED | |
| **AE Stopped Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | Moderate |
| **Relation to Study Drug by Investigator** | Reasonable Possibility |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | OTHER MEDICALLY IMPORTANT SERIOUS EVENT |

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

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M15-572

治験責任医師からの報告。本被験者はカナダの 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，皮膚の基底細胞癌の事象を発現した。

**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，非喫煙者及び元飲酒者（1 日 2～4 杯）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象の診断日が，盲検化された皮下注製剤の最終投与日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は皮膚の基底細胞癌を発現した。

被験者は背部の皮膚病変に対し電気凝固術と掻爬による切除生検を受けた。

**The patient's past medications include:**

DESONIDE for PSORIASIS (19[redacted] - [redacted] 20[redacted])

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

CLOBEX for PSORIASIS (20[redacted] - [redacted] 20[redacted])

DOVOBET for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Basal cell carcinoma (10004146) (Basal cell carcinoma (10004146) ) [v.23.0] [10004146]

**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 BASAL CELL CARCINOMA OF THE SKIN

**- Investigator:** Not applicable

**- AbbVie:** Basal cell carcinoma is common in the general white population of North America with a lifetime risk of development of 30 percent.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] SKIN BIOPSY:** results not provided

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 |
|---|---|---|---|---|
| 心膜炎 | X | | | X |

| Treatment Group | Age at Study Start | Sex | Race |
|---|---|---|---|
| ADA 40 mg EOW | 5[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| OTHER: CAT ALLERGY | 19[redacted] |
| OTHER: ENVIRONMENTAL ALLERGIES | 19[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| DEGENERATIVE DISC DISEASE: C4-C6 DEGENERATIVE CHANGES | 20[redacted] |
| OTHER: DYSPHAGIA | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OTHER: MENOPAUSE | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: GASTROSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | CURRENT | 0.5 PACK | 30 | |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 171 | 171 |
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 172 | [redacted]20[redacted] / 392 | 221 |
| ADA | 40MG | SC | EOW | [redacted]20[redacted] / 393 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| NAPHCON-A | 2 OTHER: DROPS | PRN | Y-M: 19[redacted] |
| SALBUTAMOL | 100 ug | PRN | Y-M: 19[redacted] |
| BETAMETHASONE | 1 OTHER: APPLICATION | PRN | Y-M: 20[redacted] |
| IBUPROFEN | 400 mg | PRN | Y-M: 20[redacted] |
| ARTHROTEC | 75/200 OTHER: MG/MCG | BID | Y-M: 20[redacted] |
| HYDROCORTISONE | 1 OTHER: APPLICATION | PRN | Y-M: 20[redacted] |
| NAPROXEN | 500 mg | PRN | Y-M: 20[redacted] |
| ARTHROTEC | 50/200 OTHER: MG/MCG | BID | Y-M: 20[redacted] |
| FOLIC ACID | 5 mg | OTHER: 6 DAYS PER WEEK | Y-M: 20[redacted] |
| METHOTREXATE | 15 mg | EVERY WEEK | Y-M: 20[redacted] |
| PANADEINE CO | 1 OTHER: TABLET | PRN | Y-M: 20[redacted] |
| METHOTREXATE | 25 mg | EVERY WEEK | Y-M: 20[redacted] |
| SULFASALAZINE | 500 mg | BID | Y-M: 20[redacted] / -312 |
| SULFASALAZINE | 1000 mg | BID | Y-M: 20[redacted] / -305 |

**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 |
|---|---|---|---|---|
| NAPHCON-A | 2 OTHER: DROPS | PRN | Y-M: 19[redacted] | NOT REPORTED |
| SALBUTAMOL | 100 ug | PRN | Y-M: 19[redacted] | Y-M: 20[redacted] / 652 |
| NAPROXEN | 500 mg | PRN | Y-M: 20[redacted] | Y-M: 20[redacted] / 652 |
| FOLIC ACID | 5 mg | OTHER: 6 DAYS PER WEEK | Y-M: 20[redacted] | NOT REPORTED |
| METHOTREXATE | 25 mg | EVERY WEEK | Y-M: 20[redacted] | NOT REPORTED |
| SULFASALAZINE | 1000 mg | BID | Y-M: 20[redacted] / -305 | NOT REPORTED |
| ACETYLSALICYLIC ACID | 162 mg | OTHER: ONCE | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 653 |
| COLCHICINE | 1.2 mg | BID | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 653 |
| DIMENHYDRINATE | 50 mg | OTHER: ONCE | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 653 |
| KETOROLAC | 30 mg | OTHER: ONCE | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 653 |
| MAGNESIUM SULFATE | 2 g | OTHER: ONCE | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 653 |
| MORPHINE | 2.5 mg | BID | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 653 |

| | | | | |
|---|---|---|---|---|
| IPRATROPIUM | 500 ug | OTHER: Q6H | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 655 |
| SALBUTAMOL | 2.5 mg | OTHER: Q6H | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 655 |
| DALTEPARIN | 5000 IU | QD | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 656 |
| KETOROLAC | 10 mg | QID | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 656 |
| NICOTINE | 14 mg | QD | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 708 |
| MONTELUKAST | 10 mg | QD | Y-M: 20[redacted] / 653 | Y-M: 20[redacted] / 753 |
| ULTRACET | 2 OTHER: TABLET | OTHER: Q6H | Y-M: 20[redacted] / 654 | Y-M: 20[redacted] / 655 |
| OMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted] / 654 | Y-M: 20[redacted] / 656 |
| COLCHICINE | 0.6 mg | BID | Y-M: 20[redacted] / 654 | Y-M: 20[redacted] / 753 |
| PANTOPRAZOLE | 80 mg | OTHER: ONCE | Y-M: 20[redacted] / 656 | Y-M: 20[redacted] / 658 |
| AZITHROMYCIN | 500 mg | OTHER: ONCE | Y-M: 20[redacted] / 657 | Y-M: 20[redacted] / 657 |
| FUROSEMIDE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 657 | Y-M: 20[redacted] / 657 |
| RED BLOOD CELLS | 1 OTHER: UNIT | OTHER: ONCE | Y-M: 20[redacted] / 657 | Y-M: 20[redacted] / 657 |
| HYDROMORPHONE | 0.5 mg | OTHER: Q2H | Y-M: 20[redacted] / 657 | Y-M: 20[redacted] / 658 |
| KETOROLAC | 30 mg | OTHER: Q8H | Y-M: 20[redacted] / 657 | Y-M: 20[redacted] / 658 |
| CEFUROXIME | 2 g | QD | Y-M: 20[redacted] / 657 | Y-M: 20[redacted] / 661 |
| CLARITHROMYCIN | 250 mg | QD | Y-M: 20[redacted] / 657 | Y-M: 20[redacted] / 662 |
| ACETYLSALICYLIC ACID | 650 mg | TID | Y-M: 20[redacted] / 657 | Y-M: 20[redacted] / 753 |
| ULTRACET | 2 OTHER: TABLET | PRN | Y-M: 20[redacted] / 658 | Y-M: 20[redacted] / 659 |
| OMEPRAZOLE | 20 mg | BID | Y-M: 20[redacted] / 660 | Y-M: 20[redacted] / 798 |
| BENZOCAINE | 1 OTHER: SPRAY | OTHER: ONCE | Y-M: 20[redacted] / 661 | Y-M: 20[redacted] / 661 |
| FENTANYL | 50 ug | OTHER: ONCE | Y-M: 20[redacted] / 661 | Y-M: 20[redacted] / 661 |
| MIDAZOLAM | 3 mg | OTHER: ONCE | Y-M: 20[redacted] / 661 | Y-M: 20[redacted] / 661 |
| SALBUTAMOL | 2 OTHER: PUFFS | PRN | Y-M: 20[redacted] / 662 | NOT REPORTED |
| CLONIDINE | 0.1 mg | QD | Y-M: 20[redacted] / 713 | Y-M: 20[redacted] / 743 |
| GABAPENTIN | 100 mg | BID | Y-M: 20[redacted] / 723 | Y-M: 20[redacted] / 753 |

| | | | | |
|---|---|---|---|---|
| VENLAFAXINE | 37.5 mg | QD | Y-M: 20[redacted] / 747 | Y-M: 20[redacted] / 760 |
| NAPROXEN | 500 mg | BID | Y-M: 20[redacted] / 775 | Y-M: 20[redacted] / 804 |
| RABEPRAZOLE | 20 mg | BID | Y-M: 20[redacted] / 799 | Y-M: 20[redacted] / 821 |

**Event #2: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events**

| | |
|---|---|
| **Event Description** | PERICARDITIS |
| **Preferred term** | 心膜炎 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 653 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 658): Alanine Aminotransferase: 35 [0 - 25] U/L; Albumin: 26 [33 - 45] G/L; Alkaline Phosphatase: 198 [30 - 120] U/L; Basophils: 0.01 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.1 [0 - 1] %; Calcium: 2.31 [2.1 - 2.6] MMOL/L; Chloride: 101 [97 - 106] MMOL/L; Creatinine: 54 [35 - 97] UMOL/L; Eosinophils: 0.2 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 2.6 [0 - 5] %; Erythrocytes: 4 [3.8 - 5.2] 10^12/L; Hematocrit: 0.39 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 127 [120 - 160] G/L; Leukocytes: 7.6 [4.5 - 11] 10^9/L; Lymphocytes: 1.39 [1.3 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 18.3 [22 - 52] %; Monocytes: 1.06 [0.3 - 0.8] 10^9/L; Monocytes/Leukocytes: 13.9 [5 - 12] %; NPTST099-BILIRUBIN DIRECT: 4 [0 - 7] UMOL/L; NPTST100-BILIRUBIN TOTAL: 10 [5 - 21] UMOL/L; NPTST194-CORRECTED CALCIUM: 2.59 [2.1 - 2.6] MMOL/L; NPTST298-GGT: 99 [5 - 29] U/L; NPTST370-IMMATURE GRANS: 0.4 [NOT REPORTED - NOT REPORTED] %; NPTST371-IMMATURE GRANS ABS: 0.03 [NOT REPORTED - NOT REPORTED] 10^9/L; NPTST412-LIPASE: 21 [0 - 60] U/L; NPTST422-MAGNESIUM: 0.82 [0.7 - 0.96] MMOL/L; NPTST427-MCH: 32.1 [26 - 34] PG; NPTST428-MCHC: 326 [320 - 365] G/L; NPTST429-MCV: 98.5 [80 - 98] FL; NPTST454-MPV: 9.8 [9.4 - 12.4] FL; NPTST510-PHOSPHATE: 0.94 [0.81 - 1.45] MMOL/L; NPTST533-PROTEIN TOTAL: 64 [60 - 80] G/L; NPTST562-RDW: 14.6 [11.4 - 14.4] %; NPTST662-UREA: 5.2 [2.8 - 7.1] MMOL/L; Neutrophils: 4.92 [1.8 - 5.4] 10^9/L; Neutrophils/Leukocytes: 64.7 [34 - 68] %; Platelets: 274 [140 - 440] 10^9/L; Potassium: 4.2 [3.5 - 5.1] MMOL/L; Sodium: 142 [135 - 147] MMOL/L; [redacted]20[redacted] (RX DAY 659): Alanine Aminotransferase: 32 [0 - 25] U/L; Albumin: 28 [33 - 45] G/L; Alkaline Phosphatase: 183 [30 - 120] U/L; Basophils: 0.01 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.2 [0 - 1] %; Chloride: 101 [97 - 106] MMOL/L; Creatinine: 53 [35 - 97] UMOL/L; Eosinophils: 0.22 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 3.4 [0 - 5] %; Erythrocytes: 4.3 [3.8 - 5.2] 10^12/L; Hematocrit: 0.15 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 142 [120 - 160] G/L; Leukocytes: 6.4 [4.5 - 11] 10^9/L; Lymphocytes: 1.79 [1.3 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 27.8 [22 - 52] %; Monocytes: 0.61 [0.3 - 0.8] 10^9/L; Monocytes/Leukocytes: 9.5 [5 - 12] %; NPTST099-BILIRUBIN DIRECT: 3 [0 - 7] UMOL/L; NPTST100-BILIRUBIN TOTAL: 5 [5 - 21] UMOL/L; NPTST129-C-REACTIVE PROTEIN: 92 [0 - 5] MG/L; NPTST298-GGT: 91 [5 - 29] U/L; NPTST370-IMMATURE GRANS: 0.2 [NOT REPORTED - NOT REPORTED] %; NPTST370-IMMATURE GRANS: 0.01 [NOT REPORTED - NOT REPORTED] 10^9/L; NPTST412-LIPASE: 23 [0 - 60] U/L; NPTST427-MCH: 33.3 [26 - 34] PG; NPTST428-MCHC: 341 [320 - 365] G/L; NPTST429-MCV: 97.4 [80 - 98] FL; NPTST454-MPV: 9.2 [9.4 - 12.4] FL; NPTST533-PROTEIN TOTAL: 69 [60 - 80] G/L; NPTST562-RDW: 14.2 [11.4 - 14.4] %; NPTST662-UREA: 5 [2.8 - 7.1] MMOL/L; Neutrophils: 3.8 [1.8 - 5.4] 10^9/L; Neutrophils/Leukocytes: 58.9 [34 - 68] %; Platelets: 308 [140 - 440] 10^9/L; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Sodium: 146 [135 - 147] MMOL/L; [redacted]20[redacted] (RX DAY 660): Alanine Aminotransferase: 29 [0 - 25] U/L; Albumin: 28 [33 - 45] G/L; Alkaline Phosphatase: 162 [30 - 120] U/L; Basophils: 0.02 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 1] %; Calcium: 2.35 [2.1 - 2.6] MMOL/L; Chloride: 100 [97 - 106] MMOL/L; Creatinine: 58 [35 - 97] UMOL/L; Eosinophils: 0.24 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 3.8 [0 - 5] %; Erythrocytes: 4.2 [3.8 - 5.2] 10^12/L; Hematocrit: 0.4 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 135 [120 - 160] G/L; Leukocytes: 6.3 [4.5 - 11] 10^9/L; Lymphocytes: 2.02 [1.3 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 32.2 [22 - 52] %; Monocytes: 0.56 [0.3 - 0.8] 10^9/L; Monocytes/Leukocytes: 8.9 [5 - 12] %; NPTST099-BILIRUBIN DIRECT: 2 [0 - 7] UMOL/L; NPTST100-BILIRUBIN TOTAL: 5 [5 - 21] UMOL/L; NPTST129-C-REACTIVE PROTEIN: 57 [0 - 5] MG/L; NPTST194-CORRECTED CALCIUM: 2.59 [2.1 - 2.6] MMOL/L; NPTST298-GGT: 81 [5 - 29] U/L; NPTST412-LIPASE: 21 [0 - 60] U/L; NPTST422-MAGNESIUM: 0.73 [0.7 - 0.96] MMOL/L; NPTST510-PHOSPHATE: 1.07 [0.81 - 1.45] MMOL/L; NPTST533-PROTEIN TOTAL: 67 [60 - 80] G/L; NPTST662-UREA: 4.8 [2.8 - 7.1] MMOL/L; Neutrophils: 3.41 [1.8 - 5.4] 10^9/L; Neutrophils/Leukocytes: 54.5 [34 - 68] %; Platelets: 324 [140 - 440] 10^9/L; Potassium: 4.2 [3.5 - 5.1] MMOL/L; Sodium: 143 [135 - 147] MMOL/L; [redacted]20[redacted] (RX DAY 661): Alanine Aminotransferase: 37 [0 - 25] U/L; Albumin: 30 [33 - 45] G/L; Alkaline Phosphatase: 164 [30 - 120] U/L; Basophils: 0.02 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 1] %; Calcium: 2.36 [2.1 - 2.6] MMOL/L; Chloride: 102 [97 - 106] MMOL/L; Creatinine: 61 [35 - 97] UMOL/L;

Eosinophils: 0.2 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 2.6 [0 - 5] %; Erythrocytes: 4.4 [3.8 - 5.2] 10^12/L; Hematocrit: 0.44 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 142 [120 - 160] G/L; Leukocytes: 7.6 [4.5 - 11] 10^9/L; Lymphocytes: 1.96 [1.3 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 25.7 [22 - 52] %; Monocytes: 0.64 [0.3 - 0.8] 10^9/L; Monocytes/Leukocytes: 8.4 [5 - 12] %; NPTST101-BILIRUBIN, DIRECT: 2 [0 - 7] UMOL/L; NPTST102-BILIRUBIN,TOTAL: 4 [5 - 21] UMOL/L; NPTST129-C-REACTIVE PROTEIN: 42 [0 - 5] MG/L; NPTST194-CORRECTED CALCIUM: 2.56 [2.1 - 2.6] MMOL/L; NPTST298-GGT: 81 [5 - 29] U/L; NPTST412-LIPASE: 31 [0 - 60] U/L; NPTST422-MAGNESIUM: 0.76 [0.7 - 0.96] MMOL/L; NPTST427-MCH: 32.2 [26 - 34] PG; NPTST428-MCHC: 321 [320 - 365] G/L; NPTST429-MCV: 100.5 [80 - 98] FL; NPTST454-MPV: 9.6 [9.4 - 12.4] FL; NPTST510-PHOSPHATE: 1 [0.81 - 1.45] MMOL/L; NPTST562-RDW: 13.7 [11.4 - 14.4] %; NPTST662-UREA: 5 [2.8 - 7.1] MMOL/L; Neutrophils: 4.8 [1.8 - 5.4] 10^9/L; Neutrophils/Leukocytes: 62.7 [34 - 68] %; Platelets: 353 [140 - 440] 10^9/L; Potassium: 4.1 [3.5 - 5.1] MMOL/L; Protein: 73 [60 - 80] G/L; Sodium: 145 [135 - 147] MMOL/L

**Microbiology**

[redacted]20[redacted] (RX DAY 657): BLOOD NPTST108-BLOOD CULTURE LEFT ARM: Negative-NO ORGANISMS FOLLOWING 5 DAYS OF INCUBATION; BLOOD NPTST111-BLOOD CULTURE RIGHT ARM: Negative-NO ORGANISMS FOLLOWING 5 DAYS OF INCUBATION; OTHER PERICARDIAL FLUID NPTST271-FLUID CULTURE FOR ACID-FAST BAC: Negative-NO ACID-FAST BACILLI OBSERVED; OTHER PERICARDIAL FLUID NPTST272-FLUID FOR ANAEROBES: Negative-NO ANAEROBES ISOLATED; OTHER PERICARDIAL FLUID NPTST273-FLUID FOR CULTURE: Negative-NO ORGANISMS ISOLATED; [redacted]20[redacted] (RX DAY 661): OTHER MUCOSA NPTST317-HELICOBACTER PYLORI RAPID UREAS: Negative

**SAE Supplemental Procedure**

[redacted]20[redacted] (RX DAY 653): CHEST X-RAY: NEW FINDING OF DIFFUSE CARDIAC ENLARGEMENT. THE POSSIBILITY OF A PERICARDIAL EFFUSION MAY BE CONSIDERED.; [redacted]20[redacted] (RX DAY 654): ECHOCARDIOGRAPHY: MODERATE-SIZED CIRCUMFERENTIAL PERICARDIAL EFFUSION WITH EARLY ECHOCARDIOGRAPHIC FEATURES OF TAMPONADE; [redacted]20[redacted] (RX DAY 655): CHEST X-RAY: NEW OPACITY IN THE LEFT LOWER LUNG ZONE ASSOCIATED WITH MILD PLEURAL EFFUSION. THE DIFFERENTIAL DIAGNOSIS INCLUDES ACTELECTASIS AND PNEUMONIA.; [redacted]20[redacted] (RX DAY 656): ABDOMINAL ULTRASOUND: CONGESTIVE HEPATOMEGALY IS SUSPECTED. NO EVIDENCE OF CHOLELITHIASIS/INTRAHEPATIC BILIARY DILATATION; [redacted]20[redacted] (RX DAY 657): ABDOMINAL X-RAY: FECAL RESIDUE AND GAS THROUGHOUT NONDISTENDED COLON. NO BOWEL OBSTRUCTION AND NO FREE AIR. NO ABNORMAL SOFT TISSUE MASSES OR CACLIFICATIONS; CHEST AP X-RAY: COMPARED TO PREVIOUS STUDY FROM THE SAME DAY. HEART REMAINS DIFFUSELY ENLARGED. SOME OF THE LINEAR ATELECTASIS IN THE LEFT MID TO LOWER LUNG HAS RESOLVED. A SMALLER PLEURAL EFFUSION IS SEEN ON THELEFT. NO NEW CONSOLIDATION OR ATELECTASIS. NO NEW ACUTE PROCESS OTHERWISE; CHEST X-RAY: PERSISTENT CARDIAC CONTOUR ENLARGEMENT IN THIS PATIENT WITH KNOWN PERICARDIAL EFFUSION, NOT SIGNIFICANTLY IMPROVED. A MODERATE LEFT-SIDED PLEURAL EFFUSION IS NOW PRESENT AND LINEAR DENSITIES IN THE MID TO LOWER LEFT LUNG MAY REPRESENT INCREASING ATELECTASIS IN ADDITION TO UNDERLYING SCARRING.; ECHOCARDIOGRAM-GUIDED PERICARDIOCENTESIS: PATIENT HAD CLINICAL SIGNS OF TAMPONADE. AFTER LOCALIZING THE SITE OF PUNCTURE ON THE LEFT PRECORDIUM. WE USED THE SELDINGER TECHNIQUE AND A PIGTAIL WAS INSERTED IN THE PERICARDIUM. WE MANAGED TO DRAIN 800 ML OF RED COLORED FLUID FROM THE PERICARDIUM. POST PERICARTIOCENTESIS, NO MORE PERICARDIAL EFFUSION WAS DOCUMENTED. NO COLLAPSE OF THE RIGHT VENTRICLE OR THE RIGHT ATRIUM WAS DOCUMENTED.THE LEFT VENTRICULAR EJECTION FRACTION WAS NORMAL. THERE ARE NO OBVIOUS VALVULAR ABNORMALITIES. SUCCESSFUL PERICARDIOCENTESIS UNDER ECHOCARDIOGRAPHY GUIDANCE. NO ORGANISMS FOUND IN FLUID; [redacted]20[redacted] (RX DAY 658): CHEST X-RAY: THE HEART REMAINS MINIMALLY DIFFUSELY ENLARGED. SINCE TH PREVIOUS EXAMINATION FROM THE PREVIOUS DAY, A SMALL LEFT PLEURAL EFFUSION STILL PERSISTS, MINIMALLY IMPROVED. THE ATELECTASIS IN THE LEFT LUNG BASE ALSO SHOWS SLIGHT IMPROVEMENT. THE LEFT LATERAL MIDLUNG ATELECTASIS PERSISTS. NO NEW AREAS OF CONSOLIDATION OR ATELECTASIS; [redacted]20[redacted] (RX DAY 661): CHEST/LIVER CT: MINIMAL PERICARDIAL EFFUSION ALONG THE RIGHT LOWER PERICARDIAL RECESS. MAXIMUM FLUID THICKNESS MEASURES APPROX 14 MM. MINIMAL LEFT-SIDED PLEURAL EFFUSION WITH LEFT BASAL SUBSEGMENTAL ATELECTASIS. INFERIOR, LINGULA SUBSEGMENTAL ATELECTASIS IS ALSO PRESENT. VISUALIZED UPPER LUNG FIELDS SHOW NO ABNORMAL OPACITY. MULTIPLE SMALL AXILLARY/MEDIASTINAL LYMPH NODES ARE NOTED WITH FATTY HILUM, THOUGHT TOBE REACTIVE. NO DESTRUCTIVE LESIONS ARE NOTED IN BONY THORACIC CAGE. FATTY LIVER IS NOTED. NO LESIONS NOTED IN THE SPLEEN, PANCREAS, ADRENAL GLANDS AND BOTH KIDNEYS; GASTROSCOPY: EROSIVE GASTRITIS DIAGNOSED; [redacted]20[redacted] (RX DAY 662):

ECHOCARDIOGRAPHY: FOLLOW-UP FOR PERICARDIAL EFFUSION. ACOUSTIC WINDOWS WERE SATISFACTORY. LEFT VENTRICULAR CAVITY NORMAL IN SIZE AND SYSTOLIC FUNCTION. NO REGIONAL WALL MOTION ABNORMALITIES, WALL THICKNESS NORMAL. DIASTOLIC FUNCTION INDETERMINATE. LEFT ATRIUM MILDLY DILATED. RIGHT CARDIAC CHAMBERS NORMAL IN SIZE WITH NORMAL RIGHT VENTRICULAR SYSTOLIC FUNCTION. ALL CARDIAC VALVES NORMAL IN MORPHOLOGY AND FUNCTION. TRIVIAL MITRAL REGURGITATION. NO TRICUSPID REGURGITATION. ASCENDING AORTA, AORTIC ROOT AND ARCH NORMAL IN SIZE. ABDOMINAL AORTA AND PULMONARY ARTERY NOT WELL VISUALIZED. IVC NORMAL IN SIZE.; ECHOCARDIOGRAPHY: (CONTINUED FROM PREVIOUS LINE): THERE IS A TRIVIAL PERICARDIAL EFFUSION WELL VISUALIZED ANTERIORLY. NO INTRACARDIAC MASS, THROMBUS OR SHUNT. IMPRESSION: 1. TRIVIAL PERICARDIAL EFFUSION WELL VISUALIZED ANTERIORLY 2.NO SIGNIFICANT VALVULAR ABNORMALITY 3. NORMAL LEFT AND RIGHT VE

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|---|---|
| **AE Stopped Rx Day** | 662 |
| **Duration of AE** | 10 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | LONG TERM SMOKER, PSORIATIC ARTHRITIS |
| **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:** M15-572

治験責任医師からの報告。本被験者はカナダの 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，心膜炎の事象を発現した。

**Event 2 の臨床経過：**

関連する病歴は，局面型乾癬，嚥下障害，胃内視鏡検査，乾癬性関節炎，閉経，現紙巻タバコ喫煙者（1 日 0.5 箱を 30 年間），現飲酒者（1 日 2 杯未満），軽度の慢性閉塞性肺疾患，胃炎，脳卒中の家族歴及び離婚であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は心膜炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，心膜炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は入院前日からの咽喉痛及び胸痛のため来院した。特に深呼吸時に激しい痛みがあった。医療記録によると，入院理由は，左胸水を伴う心膜炎（非重篤），うっ血性肝腫大及びうっ血性心不全の諸症状（非重篤）であった。入院中，基礎治療薬の投与は継続された。20[redacted] 年 [redacted] 月 [redacted] 日，心エコーガイド下で穿刺が行われ，800 mL の胸水が除去された。除去された胸水に病原菌は認められなかった。バイタルサインは入院期間を通して正常であった。心嚢水やタンポナーデは認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，胃内視鏡検査が行われ，びらん性胃炎（非重篤）と診断された。血液生化学検査及び血液学的検査の結果は正常であった。除去された心嚢液に病原菌は認められなかった。CT スキャン検査で，ごくわずかな左側胸水（非重篤），下縦舌筋，小腋窩リンパ節及び縦隔リンパ節の左亜区域性無気肺（非重篤）並びに脂肪肝（非重篤）が認められた。アルカリホスファターゼ，γGT及びALTがわずかに増加していたが，いずれも心不全によるうっ血に起因するものである可能性が最も高かった。C-反応性蛋白も高値であったが，これは当初から高値であった。ウイルス培養，抗酸性桿菌培養及び血液培養の結果はまだ出ていなかった。直近の心電図検査では，洞調律は正常であり，非特異的 T 波変化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，心エコー再検査の結果は正常であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。担当医の判断では，心膜炎に続発した心嚢液貯留は乾癬性関節炎によるものである可能性が最も高かった。

投与された薬剤は，コルヒチン及び asa であった。

Causality for ABT-494 (Blinded)

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1) Pericarditis (10034484) (Pericarditis (10034484) ) [v.22.0] [10034484]

**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)

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Event of PERICARDITIS

**- Investigator:** Long term smoker, psoriatic arthritis

**- AbbVie:** Given diagnostic testing has not confirmed any identifiable cause of the pericarditis and frequently these cases are presumed to have a viral or autoimmune etiology, the event is more likely related to sore throat symptoms a day prior to admission with underlying autoimmune systemic inflammatory disease as an additional risk factor.

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 to UPA 30 mg QD | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| MIGRAINE HEADACHE | 19[redacted] |
| OTHER: HERNIA | 19[redacted] |
| HYPERTENSION | 19[redacted] |
| NEPHROLITHIASIS | 19[redacted] |
| DIABETES MELLITUS: NON-INSULIN DEPENDENT | 20[redacted] |
| OTHER: PLAQUE PSORIASIS | 20[redacted] |
| PSORIATIC ARTHRITIS | 20[redacted] |
| OSTEOARTHRITIS: LEFT KNEE | 20[redacted] |
| OTHER: COLON POLYPS - BENIGN | 20[redacted] |
| EYE DISEASE/DISORDER: LEFT MACULAR DEGENERATION | 20[redacted] |
| OTHER: NON-DISSEMINATED HERPES ZOSTER | 20[redacted] |
| OTHER: SYNOVIAL CYST LEFT SECOND DISTAL INTERPHALANGEAL (FINGER) | 20[redacted] |
| LIVER DISEASE (EXCLUDING HEPATITIS): FATTY LIVER | 20[redacted] |
| OTHER: BENIGN PULMONARY NODULES | 20[redacted] |
| OTHER: LOW B12 | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: HERNIA REPAIR | 19[redacted] |
| SURGERY: ROUTINE COLONOSCOPY | 20[redacted] |
| SURGERY: COLONOSCOPY WITH POLYPECTOMY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 33 | 19[redacted] |
| CIGARS | NEVER | | | |
| E-CIGARETTES | NEVER | | | |
| PIPES | NEVER | | | |

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

**Study Drug Administration**

| Study Drug | Dose/Units | Route | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| PLACEBO | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 167 | 167 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 168 | [redacted]20[redacted] / 393 | 226 |
| ABT-494 | 30 MG | ORAL | QD | [redacted]20[redacted] / 394 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| APREMILAST | 30 mg | BID | Y-M: 20[redacted] |
| NAPROXEN | 500 mg | QD | Y-M: 20[redacted] |
| HEPATITIS B IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| TRIAMCINOLONE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] |
| TRIAMCINOLONE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] |
| ERGOCALCIFEROL | 1000 IU | QD | Y-M: 20[redacted] |
| TRIAMCINOLONE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] |
| METFORMIN | 1 g | BID | Y-M: 20[redacted] |
| CURCUMA LONGA | 1 OTHER: CAPSULE | BID | Y-M: 20[redacted] |
| CO-DIOVAN | 12.5/160 OTHER: MG/MG | QD | Y-M: 20[redacted] |
| VITEYES | 10/2 OTHER: MG/MG | BID | Y-M: 20[redacted] |
| IBUPROFEN | 400 mg | PRN | Y-M: 20[redacted] / -232 |
| CYANOCOBALAMIN | 1000 mg | QD | Y-M: 20[redacted] / -120 |
| BLOPRESS PLUS | 16/12.5 OTHER: MG/MG | QD | Y-M: 20[redacted] / -39 |

**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 |
|---|---|---|---|---|
| ERGOCALCIFEROL | 1000 IU | QD | Y-M: 20[redacted] | NOT REPORTED |
| METFORMIN | 1 g | BID | Y-M: 20[redacted] | NOT REPORTED |
| CURCUMA LONGA | 1 OTHER: CAPSULE | BID | Y-M: 20[redacted] | NOT REPORTED |
| VITEYES | 10/2 OTHER: MG/MG | BID | Y-M: 20[redacted] | NOT REPORTED |
| IBUPROFEN | 400 mg | PRN | Y-M: 20[redacted] / -232 | NOT REPORTED |
| CYANOCOBALAMIN | 1000 mg | QD | Y-M: 20[redacted] / -120 | NOT REPORTED |
| BLOPRESS PLUS | 16/12.5 OTHER: MG/MG | QD | Y-M: 20[redacted] / -39 | NOT REPORTED |
| LIDOCAINE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] / 251 | Y-M: 20[redacted] / 251 |
| TRIAMCINOLONE | 80 mg | OTHER: ONCE | Y-M: 20[redacted] / 251 | Y-M: 20[redacted] / 251 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENED OSTEOARTHRITIS LEFT KNEE |
| **Preferred term** | 変形性関節症 |
| **AE Onset Date / Rx Day** | [redacted]20[redacted] / 198 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **SAE Supplemental Procedure** | |
| [redacted]20[redacted] (RX DAY 531): STANDING KNEES X-RAY: MODERATELY SEVERE OSTEOARTHRITIC CHANGES ARE PRESENT IN THE LEFT KNEE MEDIAL COMPARTMENT WITH MILD INVOLVEMENT OF THE LATERAL AND PATELLOFEMORAL. NO JOINT EFFUSION IS PRESENT. THE RIGHT KNEE MEDIALLATERAL COMPARTMENTS ARE UNREMARKABLE WITH NO ARTHRITIC CHANGES DETECTED; [redacted]20[redacted] (RX DAY 533): LEFT TOTAL KNEE ARTHROPLASTY: SUCCESSFUL, NO COMPLICATIONS | |
| **AE Stopped Rx Day** | 533 |
| **Duration of AE** | 336 DAYS |
| **Severity** | Severe |
| **Relation to Study Drug by Investigator** | No Reasonable Possibility |
| **Investigator Alternative Etiology** | PROGRESSION OF PRE-EXISTING DISEASE, AGE, OBESITY |
| **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:** M15-572

治験責任医師からの報告。本被験者はカナダの 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，左膝の変形性関節症の悪化の事象を発現した。

**Event 1 の臨床経過：**

関連する病歴は，インスリン非依存性糖尿病，乾癬性関節炎，左膝の変形性関節症，元紙巻タバコ喫煙者（1 日 1 箱を 33 年間，19[redacted] 年に禁煙）及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。手術前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左膝の変形性関節症の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左膝の変形性関節症の悪化は消失した。

入院前，動作に伴う疼痛の増強，睡眠の中断，著明な内反マルアライメント及び鎮痛歩行が認められていた。手術前の 1 年間，被験者の症状は悪化し続け，整形外科医に紹介された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は外科医の診察を受け，手術が予定された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，同日に左膝の全膝関節形成術を受けた。手術は成功し合併症もなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for UPADACITINIB (Blinded)

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1) Osteoarthritis aggravated (10031162) (Osteoarthritis (10031161) ) [v.22.1] [10031162]

**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)

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Event of WORSENED OSTEOARTHRITIS LEFT KNEE

**- Investigator:** PROGRESSION OF PRE-EXISTING DISEASE

**- AbbVie:** event is more likely related to pre-existing osteoarthritis.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] [redacted] **20[redacted] X-RAY KNEE:** standing knee xray: Moderately severe osteoarthritic changes are present in the left knee medial compartment with mild involvement of the lateral and patellofemoral. No joint effusion is present. The right knee medial lateral compartments are unremarkable with no arthritic changes detected