M21-561 試験

治験の標題： ウパダシチニブ 15 mg 製剤 3 錠としてウパダシチニブを 45 mg 投与したときのバイオアベイラビリティをウパダシチニブ 45 mg 製剤 1 錠と比較して評価する第 I 相試験	
施設数/実施国名： 多施設 / 米国	
治験責任医師： [redacted], MD	
公表文献 (参考資料) ： なし	
治験期間： 最初の被験者の初回来院日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ：I
目的： 高脂肪/高カロリー食後条件下及び絶食条件下において，ウパダシチニブ 15 mg 製剤 3 錠としてウパダシチニブを 45 mg 投与したときのバイオアベイラビリティをウパダシチニブ 45 mg 製剤 1 錠と比較して評価する。	
治験方法： 単回投与，非盲検，無作為化，4 期，4 シークエンス，多施設のクロスオーバー試験を実施した。ウパダシチニブの濃度測定用の血液試料は各期の投与後 72 時間まで採取した。	
被験者数 (計画時と解析時) ： 計画時：60 名，登録：60 名，完了：59 名，安全性評価：60 名，薬物動態評価：60 名	
診断と主要な組入れ基準： スクリーニングの時点で 18 歳から 55 歳までの健康な男性及び女性被験者	
被験薬，用量 / 含量 / 濃度，投与方法： ウパダシチニブ 15 mg 錠（ER17）及びウパダシチニブ 45 mg 錠（ER19）。 治験薬は経口投与した。	
投与期間： 4 日間の間隔をあけてウパダシチニブ 45 mg を 4 回単回投与した。	
評価基準： 薬物動態： C_{max}，T_{max}，$t_{1/2}$，AUC_t，AUC_{inf}，AUC_{0-12} 及び AUC_{12-72}	
統計手法： 薬物動態： C_{max}，AUC_t，AUC_{inf}，AUC_{0-12}，AUC_{12-72} の自然対数変換値を用いて線形混合効果解析を実施した。それぞれの試験レジメンと対応する標準レジメンとの比較は本混合モデルを用いて実施した。 標準レジメンに対する試験レジメンのバイオアベイラビリティ，すなわち高脂肪/高カロリー食後又は絶食条件下での 45 mg 製剤 1 錠に対する 15 mg 製剤 3 錠のバイオアベイラビリティの評価は，C_{max}，AUC_t，AUC_{inf}，AUC_{0-12}，AUC_{12-72} の自然対数変換値の解析から得られた点推定値及びその 90%信頼区間を用いて実施した。	

要約/結論

薬物動態の結果：

Regimens Test vs. Reference	Pharmacokinetic Parameter (units)	Central Value		Relative Bioavailability	
		Test	Reference	Point Estimate	90% Confidence Interval
Regimen A vs. B	C_{max} (ng/mL)	95.1	93.0	1.023	0.943, 1.110
	AUC_t (ng•h/mL)	792	763	1.037	0.989, 1.088
	AUC_{inf} (ng•h/mL)	812	785	1.034	0.983, 1.089
	AUC_{0-12} (ng•h/mL)	573	541	1.059	0.993, 1.130
	AUC_{12-72} (ng•h/mL)	209	210	0.998	0.914, 1.090
Regimen C vs. D	C_{max} (ng/mL)	125	138	0.905	0.846, 0.969
	AUC_t (ng•h/mL)	958	950	1.008	0.961, 1.057
	AUC_{inf} (ng•h/mL)	969	965	1.004	0.962, 1.049
	AUC_{0-12} (ng•h/mL)	757	762	0.993	0.938, 1.052
	AUC_{12-72} (ng•h/mL)	192	175	1.098	1.005, 1.199

Regimen A: Single 45 mg dose administered as three 15 mg tablets of upadacitinib formulation (ER17) under fasting conditions. (Test for B).

Regimen B: Single 45 mg upadacitinib tablet formulation (ER19) administered under fasting conditions. (Reference for A).

Regimen C: Single 45 mg dose administered as three 15 mg tablets of upadacitinib formulation (ER17) after high-fat/high-calorie meal. (Test for D).

Regimen D: Single 45 mg upadacitinib tablet formulation (ER19) administered after high-fat/high-calorie meal. (Reference for C).

安全性の結果：

検討したレジメンの忍容性はおおむね良好であった。1 例が Covid-19 感染症のため試験を中止したが，本事象は治験責任医師によって治験薬と関連なしと評価された。1 例が第 1 期で臨床的に重要な可能性のある CPK 値を示したため，当該被験者は第 2 期で投薬されなかった。当該被験者の CPK は第 3 期までに正常値に低下したので，当該被験者は第 3 期から投薬を再開し，試験を完了した。その他，試験期間中に臨床的に重要なバイタルサイン及び臨床検査値異常は認められなかった。報告された有害事象に特定のパターンはなく，本試験において新たな安全性の問題は認められなかった。

結論:

絶食及び高脂肪/高カロリー食後条件下のいずれにおいても，ウパダシチニブ 15 mg 製剤（ER17）3 錠とウパダシチニブ 45 mg 製剤（ER19）1 錠は生物学的に同等であった。

M19-376 試験

治験の標題： ウパダシチニブ 45 mg 臨床試験用製剤に対する 45 mg 市販予定製剤のバイオアベイラビリティの評価及びウパダシチニブ 45 mg 市販予定製剤における食事の影響を検討する第 I 相試験	
施設数/実施国名： 1 施設 / 米国	
治験責任医師： [redacted] MD	
公表文献 (参考資料) ： なし	
治験期間： 最初の被験者の初回来院日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ：I
目的： 1. 高脂肪/高カロリー食後条件下及び絶食条件下において，ウパダシチニブ 45 mg 臨床試験用製剤に対する 45 mg 市販予定製剤のバイオアベイラビリティを評価する。 2. ウパダシチニブ 45 mg 市販予定製剤において，絶食条件下に対する高脂肪/高カロリー食後条件下でのバイオアベイラビリティを評価する。	
治験方法： 単回投与，非盲検，無作為化，4 期，4 シークエンスのクロスオーバー試験を実施した。ウパダシチニブの濃度測定用の血液試料は各期の投与後 72 時間まで採取した。	
被験者数 (計画時と解析時) ： 計画時：68 名，登録：68 名，完了：65 名，安全性評価：68 名，薬物動態評価：68 名	
診断と主要な組入れ基準： スクリーニングの時点で 18 歳から 55 歳までの健康な男性及び女性被験者	
被験薬，用量 / 含量 / 濃度，投与方法： ウパダシチニブ第 III 相試験用 45 mg 錠（ER19P）及びウパダシチニブ市販予定 45 mg 錠（ER19）。 治験薬は経口投与した。	
投与期間： 4 日間の間隔をあけてウパダシチニブ 45 mg を 4 回単回投与した。	
評価基準： 薬物動態： C_{max}，T_{max}，$t_{1/2}$，AUC_t，AUC_{inf}，AUC_{0-12} 及び AUC_{12-72}	
統計手法： 薬物動態： C_{max}，AUC_t，AUC_{inf}，AUC_{0-12}，AUC_{12-72} の自然対数変換値を用いて線形混合効果解析を実施した。それぞれの試験レジメンと対応する標準レジメンとの比較は本混合モデルを用いて実施した。 標準レジメンに対する試験レジメンのバイオアベイラビリティ，すなわち高脂肪/高カロリー食後又は絶食条件下での臨床試験製剤に対する市販予定製剤のバイオアベイラビリティの評価は，C_{max}，AUC_t，AUC_{inf}，AUC_{0-12}，AUC_{12-72} の自然対数変換値の解析から得られた点推定値及びその 90%信頼区間を用いて実施した。	

要約/結論

薬物動態の結果：

絶食及び高脂肪/高カロリー食後条件下における，ウパダシチニブ 45 mg 臨床試験用製剤に対するウパダシチニブ 45 mg 市販予定製剤のバイオアベイラビリティの点推定値及び 90%信頼区間

Regimens Test vs. Reference	Pharmacokinetic Parameter (units)	Central Values		Relative Bioavailability	
		Test	Reference	Point Estimate	90% Confidence Interval
Regimen B vs. A	C_{max}	85.7	87.9	0.975	0.918 – 1.036
	AUC_t	697	702	0.992	0.954 – 1.030
	AUC_{inf}	714	723	0.987	0.950 – 1.026
	AUC_{0-12}	515	526	0.980	0.935 – 1.027
	AUC_{12-72}	174	168	1.040	0.961 – 1.126
Regimen D vs. B	C_{max}	137	85.7	1.596	1.511 – 1.685
	AUC_t	886	697	1.272	1.225 – 1.321
	AUC_{inf}	898	714	1.258	1.212 – 1.307
	AUC_{0-12}	742	515	1.441	1.379 – 1.506
	AUC_{12-72}	137	174	0.785	0.726 – 0.850
Regimen D vs. C	C_{max}	137	134	1.019	0.971 – 1.070
	AUC_t	886	896	0.989	0.962 – 1.017
	AUC_{inf}	898	912	0.985	0.958 – 1.012
	AUC_{0-12}	742	740	1.003	0.968 – 1.039
	AUC_{12-72}	137	145	0.944	0.873 – 1.020

Regimen A: Single 45 mg dose of upadacitinib Phase 3 ER formulation administered under fasting conditions (reference for B and C).

Regimen B: Single 45 mg dose of upadacitinib market-image formulation administered under fasting conditions (test for A).

Regimen C: Single 45 mg dose of upadacitinib Phase 3 ER formulation administered after high fat/high calorie meal (test for A).

Regimen D: Single 45 mg dose of upadacitinib market-image ER formulation administered after high fat/high calorie meal (test for B and C).

Note: Outlier observations from three subjects ([redacted], [redacted] and [redacted]) are excluded.

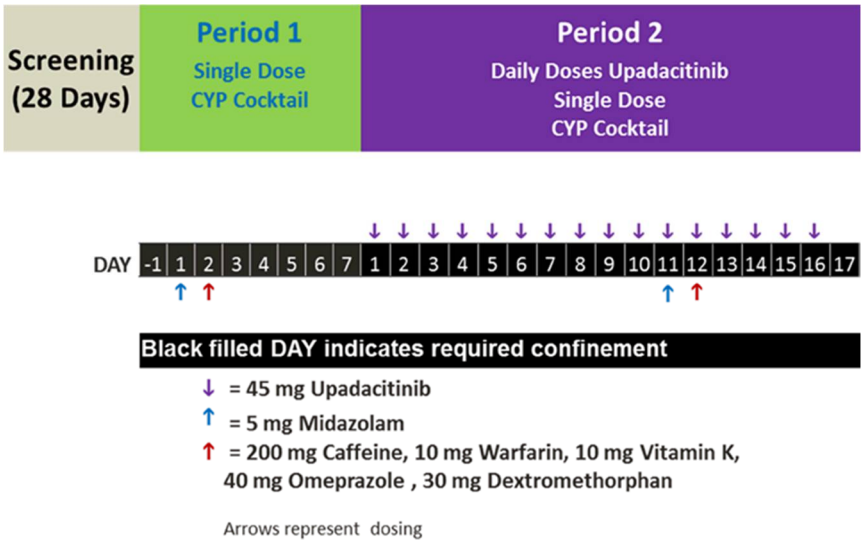
安全性の結果：

検討したレジメンの忍容性はおおむね良好であった。1 例が血中クレアチンフォスフォキナーゼ値の上昇のため試験を中止し，本事象は治験責任医師によって治験薬と関連ありと評価された。1 例が腹痛のため試験を中止したが，本事象は治験責任医師によって治験薬と関連なしと評価された。その他，試験期間中に臨床的に重要なバイタルサイン及び臨床検査値異常は認められなかった。報告された有害事象に特定のパターンはなく，本試験において新たな安全性の問題は認められなかった。

結論:

ウパダシチニブ 45 mg 市販予定製剤は，絶食及び高脂肪/高カロリー食後条件下のいずれにおいても，第 III 相試験で用いたウパダシチニブ 45 mg 臨床試験用製剤と生物学的に同等であった。ウパダシチニブ市販予定製剤を高脂肪/高カロリー食後条件下で投与したとき，絶食条件下で投与したときと比較して，C_{max} は 60%，AUC_{inf} は 26%高値を示した。

M19-139 試験

治験の標題： 健康成人被験者を対象にウパダシチニブを 45 mg の用量で 1 日 1 回反復投与したとき，ウパダシチニブがチトクロム P450 基質の薬物動態に及ぼす影響を評価する第 I 相試験	
施設数/実施国名： 1 施設 / 米国	
治験責任医師： [redacted] MD	
公表文献 (参考資料) ： なし	
治験期間： 最初の被験者の初回来院日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ：I
目的： 健康成人被験者を対象にウパダシチニブ徐放性製剤を 45 mg の用量で 1 日 1 回反復投与したとき，ウパダシチニブがチトクロム P450 基質の薬物動態に及ぼす影響を評価する。	
治験方法： 非盲検，二期，単群，反復投与試験  ピリオド 1 における最後の CYP カクテル投与とピリオド 2 における最初のウパダシチニブ投与の間には，6 日間のウォッシュアウト期間を設けた。CYP プローブ基質の濃度測定のための血液検体は，各ピリオドにおける投与後 120 時間にわたって採取した。デキストロメトルファン及びデキストロルファン濃度測定のための尿検体は，ピリオド 1 の Day 2 及びピリオド 2 の Day 12 の投与後 0-6 時間及び 6-12 時間に採取した。ウパダシチニブ濃度測定のための血液検体は，ピリオド 2 の Day 10 に 24 時間にわたって採取した。	
被験者数 (計画時と解析時) ： 計画時：20 名，登録：20 名，完了：19 名，安全性評価：20 名，薬物動態評価：19 名	
診断と主要な組入れ基準：	

18 歳から 55 歳までの健康な男性及び女性被験者
被験薬，用量 / 含量 / 濃度，投与方法： ウパダシチニブ 45 mg フィルムコート徐放錠 カフェイン 200 mg コーティング錠 ワルファリンナトリウム 10 mg 錠 ビタミン K（フィトナジオン）10 mg，5 mg 錠 オメプラゾール 40 mg 徐放カプセル ミダゾラム塩酸塩 5 mg/mL，2 mg/mL シロップ デキストロメトルファン臭化水素酸塩 30 mg/15 mL，15 mg/15 mL 液 治験薬は経口投与した。
投与期間： ミダゾラム，カフェイン，ワルファリン，ビタミン K，オメプラゾール及びデキストロメトルファンはピリオド 1 及びピリオド 2 にそれぞれ単回投与した。また，ウパダシチニブは 1 日 1 回 16 日間反復投与した。
評価基準： 薬物動態： C_{max}，T_{max}，$t_{1/2}$，AUC_t，AUC_{inf}，CL/F，AUC_{24}（ウパダシチニブのみ），未変化体に対する代謝物の AUC 比及び尿中モル回収率（R_u）
統計手法： 薬物動態： ウパダシチニブの 45 mg 1 日 1 回反復投与がカフェイン，ワルファリン，オメプラゾール及びデキストロメトルファンの薬物動態に与える影響を評価するため，ピリオド 1 の Day 2 及びピリオド 2 の Day 12 から得られた C_{max} 及び AUC を自然対数変換し，反復測定分析を実施した。 また，ウパダシチニブがミダゾラムの薬物動態に与える影響を評価するために，ピリオド 1 の Day 1 及びピリオド 2 の Day 11 から得られたデータを自然対数変換し，同様な解析を実施した。 オメプラゾールに対する 5-ヒドロキシオメプラゾールの AUC 比及びデキストロルファンに対するデキストロメトルファンの尿中のモル比についても，同様な解析を行った。

要約/結論

薬物動態の結果：

Regimens Test vs. Reference	Pharmacokinetic Parameter	Central Value		Relative Bioavailability	
		Test	Reference	Point Estimate	90% Confidence Interval
		Midazolam (CYP3A Probe Substrate)			
Administration with Upadacitinib[a] vs. Administration without Upadacitinib[b]	C_{max}	16.7	22.2	0.753	0.686, 0.825
	AUC_t	43.1	56.9	0.758	0.694, 0.829
	AUC_∞	44.7	59.0	0.757	0.694, 0.826
		Caffeine (CYP1A2 Probe Substrate)			
Administration with Upadacitinib[c] vs. Administration without Upadacitinib[d]	C_{max}	4880	4640	1.051	0.967, 1.142
	AUC_t	49800	47800	1.040	0.960, 1.126
	AUC_∞	52300	50400	1.038	0.950, 1.134
		S-Warfarin (CYP2C9 Probe Substrate)			
Administration with Upadacitinib[c] vs. Administration without Upadacitinib[d]	C_{max}	631	535	1.180	1.050, 1.327
	AUC_t	19600	17300	1.133	1.043, 1.230
	AUC_∞	22600	20100	1.121	1.045, 1.202
		R-Warfarin			
Administration with Upadacitinib[c] vs. Administration without Upadacitinib[d]	C_{max}	655	555	1.180	1.073, 1.298
	AUC_t	29400	27000	1.087	1.007, 1.173
	AUC_∞	37000	33800	1.095	1.020, 1.176
		Dextromethorphan (CYP2D6 Probe Substrate)			
Administration with Upadacitinib[c] vs. Administration without Upadacitinib[d]	C_{max}	1.65	1.27	1.299	1.126, 1.498
	AUC_t	17.2	12.7	1.358	1.178, 1.567
	AUC_∞	19.7	14.6	1.348	1.177, 1.543
		Omeprazole			
Administration with Upadacitinib[c] vs. Administration without Upadacitinib[d]	C_{max}	381	491	0.776	0.575, 1.046
	AUC_t	895	1040	0.863	0.713, 1.044
	AUC_∞	1050	1070	0.979	0.846, 1.132

薬物動態の結果（続き）：

Regimens Test vs. Reference	Pharmacokinetic Parameter	Central Value		Relative Bioavailability	
		Test	Reference	Point Estimate	90% Confidence Interval
		5-Hydroxy-Omeprazole			
Administration with Upadacitinib[c] vs. Administration without Upadacitinib[d]	C_{max}	312	377	0.828	0.696, 0.986
	AUC_t	906	1030	0.881	0.790, 0.983
	AUC_∞	968	1040	0.933	0.871, 0.999
	5-Hydroxy-Omeprazole to Omeprazole AUC Ratio (CYP2C19 Activity Marker)				
Administration with Upadacitinib[c] vs. Administration without Upadacitinib[d]	M/P AUC_t Ratio	1.01	0.991	1.022	0.935, 1.117
	M/P AUC_∞ Ratio	0.934	0.995	0.956	0.899, 1.017
	Dextromethorphan to Dextrorphan Molar Urine Recovery Ratio (CYP2D6 Activity Marker)				
Administration with Upadacitinib[c] vs. Administration without Upadacitinib[d]	DEM/DEX Ratio (0 - 12 h)	0.381	0.249	1.531	1.262, 1.857

a. Period 2 Day 11 (P2D11): midazolam 5 mg + Upadacitinib 45 mg QD (test).

b. Period 1 Day 1 (P1D1): midazolam 5 mg (reference).

c. Period 2 Day 12 (P2D12): CYP cocktail (caffeine 200 mg + omeprazole 40 mg + warfarin 10 mg + dextromethorphan 30 mg) + Upadacitinib 45 mg QD (test).

d. Period 1 Day 2 (P1D2): CYP cocktail (caffeine 200 mg + omeprazole 40 mg + warfarin 10 mg + dextromethorphan 30 mg) (reference).

安全性の結果：

検討された治験薬は，被験者の 50%において軽度の傾眠が報告されたミダゾラムを除き，おおむね良好な忍容性を示した。本試験期間中に臨床的に意義があると判断されるバイタルサイン，心電図及び臨床検査値異常は認められなかった。本試験で新たな安全性の問題は認められなかった。

結論:

ウパダシチニブ 45 mg 1 日 1 回反復投与は，ミダゾラム（CYP3A の高感受性基質：AUC 及び C_{max} が約 25%低下）及びデキストロメトルファン（CYP2D6 の高感受性基質：AUC が 35%上昇，C_{max} が 30%上昇）に対して，限定的な影響を及ぼしたが， CYP1A2，CYP2C9 及び CYP2C19 の高感受性プローブ基質 / マーカーに対しては，意味のある影響を及ぼさなかった。

M14-234 試験 Substudy 1

治験の標題： 中等症から重症の活動性潰瘍性大腸炎患者を対象としたウパダシチニブ（ABT-494）の導入療法及び維持療法における安全性及び有効性を評価する多施設共同無作為化二重盲検プラセボ対照試験	
施設数 / 実施国名： 142 施設（オーストラリア，オーストリア，ベルギー，カナダ，クロアチア，チェコ共和国，エストニア，フィンランド，フランス，ドイツ，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，マレーシア，オランダ，ノルウェー，ポーランド，ポルトガル，スロバキア，南アフリカ，スイス，台湾，イギリス及び米国）	
治験調整医師： [redacted], MD, PhD, MSc	
公表文献（参考資料）： 14 報	
治験期間： 最初の被験者の初回来院日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ： 第 IIb 相
目的： 中等症から重症の活動性潰瘍性大腸炎（以下「UC」）患者を対象として，Adapted Mayo スコア（UC の活動性を評価する Physician's global assessment を除いた Mayo スコア）による寛解導入におけるウパダシチニブの用量反応，有効性及び安全性をプラセボと比較し，M14-234 試験 Substudy（以下「SS2 を含む第 III 相試験で更に評価するウパダシチニブの導入用量を決定する。	
被験者数（計画時と解析時）： 計画時：350 例（主要被験者 250 例 + 追加被験者 100 例），解析時：382 例（主要被験者 250 例 + 追加被験者 132 例）	
診断と主要な組入れ基準： 主要な選択基準：ベースライン時の年齢が 18 歳以上 75 歳以下の男女で，ベースラインの 90 日以上前に UC と診断され，スクリーニング期間中に全大腸内視鏡検査で診断が確認されると共に，現在の感染症，上皮異形成及び/又は悪性腫瘍が除外されている患者。Adapted Mayo スコアが 5–9，かつ内視鏡サブスコアが 2–3（中央判定による評価）の活動性 UC を有しており，副腎皮質ステロイド，免疫調節薬及び/又は生物学的製剤のいずれかひとつ以上に対して効果不十分，効果減弱又は不耐容である患者。健康状態にその他の問題がない患者。 主要な除外基準：クローン病と診断されている患者。劇症の大腸炎及び/又は中毒性巨大結腸症と診断されている患者。病変が直腸のみに限局している患者。結腸全摘術若しくは結腸亜全摘術，回腸瘻，Kock パウチ又は回腸ストマ造設の既往がある患者，又は腸管の手術を予定している患者。副腎皮質ステロイド，免疫調節薬等の治験実施計画書に規定された併用禁止薬を投与された患者。	
治験方法： M14-234 試験 SS 1 は，中等症から重症の活動性 UC 患者を対象と8週間の導入療法において異なる用量のウパダシチニブ（経口投与）の有効性及び安全性をプラセボと比較して評価する第 IIb 相用量探索試験であった。合計 250 例の被験者を，1 : 1 : 1 : 1 : 1 の比率でウパダシチニブの 4 用量（1 日用量：7.5 mg，15 mg，30 mg 及び 45 mg）又はプラセボのいずれかにランダム化した。また，生物学的製剤の前治療歴（あり又はなし），ベースラインでの副腎皮質ステロイドの使用（あり又はなし）及びベースラインでの Adapted Mayo スコア（7 以下又は 7 超）を因子として層別化した。M14-234 試験 SS 1 では，組み入れた被験者の約 75%が生物学的製剤に対して効果不十分，効果減弱又は不耐容であった被験者（Bio-IR）であり，約 25%が従来の治療に対して効果不十分，効果減弱又は不耐容を示すものの生物学的製剤は無効ではない被験者（Non-bio-IR）であった。ランダム化した全被験者（主要被験者）が 8 週間の導入療法期を完了した後，プラセボに対するウパダシチニブの有効性及	

び安全性の用量設定解析を実施し，M14-234　　試験 SS 2 及び 2 つ目の導入療法試験である M14-　　試験で用いる　　導入用量を設定した。解析期間中，追加被験者 132 例を M14-234 試験 SS 1 のウパダシチニブ 30 mg 1 日 1 回群（以下「30 mg 群」）及び 45 mg 1 日 1 回群（以下「45 mg 群」）にランダム化した。追加被験者を組み入れた目的は，解析期間中に試験が中断することを回避し，M14-234 試験 SS 3 で維持療法に再ランダム化される臨床的改善を達成した被験者を十分に確保することであった。

被験薬，用量，投与方法及びロット番号：

被験薬	用量	投与方法	バルクロット番号
ウパダシチニブ	7.5 mg	経口	[redacted], [redacted]
ウパダシチニブ	15 mg	経口	[redacted], [redacted], [redacted], [redacted]
ウパダシチニブ	30 mg	経口	[redacted], [redacted], [redacted], [redacted]
ウパダシチニブ	45 mg	経口	ウパダシチニブ 30 mg 錠 + ウパダシチニブ 15 mg 錠

治療期間：

8 週間

対照薬，用量，投与方法及びロット番号：

ウパダシチニブに対応する経口フィルムコート錠 バルクロット番号：[redacted], [redacted], [redacted]

評価基準：

有効性：

主要評価項目は，投与 8 週時の Adapted Mayo スコアによる臨床的寛解率（Adapted Mayo スコアが 2 以下で，排便回数サブスコア［以下「SFS」］が 1 以下，直腸出血サブスコア［以下「RBS」］が 0，かつ内視鏡サブスコアが 1 以下）とした。

投与 8 週時又は投与 2 週時（部分的 Mayo スコアによる臨床的改善率のみ）に評価した順位付き副次評価項目は，以下のとおりであった。

1. 内視鏡的改善率（内視鏡サブスコアが 0 又は 1）
2. Full Mayo スコアによる臨床的寛解率（Full Mayo スコアが 2 以下で，かついずれのサブスコアも 1 を超えない）
3. Adapted Mayo スコアによる臨床的改善率（Adapted Mayo スコアのベースラインからの減少が 2 以上かつ 30%以上，更に RBS の減少が 1 以上又は RBS が 1 以下）
4. 部分的 Mayo スコアによる臨床的改善率（内視鏡サブスコアを除いた Mayo スコアで，部分的 Mayo スコアのベースラインからの減少が 2 以上かつ 30%以上，更に RBS の減少が 1 以上又は RBS が 1 以下）
5. Full Mayo スコアのベースラインからの変化量
6. 内視鏡的寛解率（内視鏡サブスコアが 0）
7. 組織学的改善率（Geboes スコアがベースラインから減少）

薬物動態：

ウパダシチニブの血漿中濃度の平均値（標準偏差）を，用量及び前回投与からの時間ごとに要約した。

安全性：

有害事象，バイタルサイン，身体検査，臨床検査値（血液学的検査，血液生化学検査及び尿検査）及び治験薬に係る苦情を評価した。

統計手法：

有効性：

有効性の主要解析では，intent to-treat（以下「ITT」）1A 集団（用量設定解析時に M14-234 試験 SS 1 でランダム化し，治験薬［プラセボ，ウパダシチニブ 7.5 mg，15 mg，30 mg，45 mg］を 1 回以上投与した被験者）を対象

とし，Multiple Comparison Procedure-Modeling（以下「MCP-Mod」）アプローチを用いて，主要評価項目のウパダシチニブ群とプラセボ 1 日 1 回群（以下「プラセボ群」）間の比較を行った。また，投与 8 週時の主要評価項目について，MCP-Mod アプローチを用いて 4 つのウパダシチニブ群とプラセボ群間の用量反応関係を明らかにした。ウパダシチニブ群とプラセボ群間の被験者の割合の差に関する対比較は，生物学的製剤の前治療歴（あり又はなし），ベースラインでの副腎皮質ステロイドの使用（あり又はなし）及びベースラインでの Adapted Mayo スコア（7 以下又は 7 超）を層別因子とした Cochran-Mantel-Haenszel（以下「CMH」）検定を用いて実施した。更に，割合の投与群間差に関する CMH に基づいた 95%信頼区間を算出した。有効性の主要解析では，ノンレスポンダーインピュテーション（NRI）を用い，すべての欠測データを未達成例として取り扱った。

主要評価項目の感度分析は，ハイブリッド多重補完法及び欠測データを直前の評価又は測定値で補完する手法（LOCF）を用いて解析した。また，ITT1A 集団のうち，選択/除外基準を満たさなかった被験者を除外した解析も実施した。

有効性の順位付き副次評価項目のカテゴリー変数では，被験者の割合の差に関するウパダシチニブ群とプラセボ群間の対比較を，生物学的製剤の前治療歴（あり又はなし），ベースラインでの副腎皮質ステロイドの使用（あり又はなし）及びベースラインでの Adapted Mayo スコア（7 以下又は 7 超）を層別因子とした CMH 検定を用いて実施した。更に，割合の投与群間差に関する CMH に基づいた 95%信頼区間を算出した。

有効性の順位付き副次評価項目の連続変数では，投与群及び層別変数を因子，ベースライン値を共変量とした共分散分析（ANCOVA）を用いて解析した。有効性の順位付き副次評価項目のうち，繰り返し測定する連続変数の評価項目については，混合効果・反復測定モデル（以下「MMRM」）を用いて解析した。MMRM に含めるベースライン値は，性別，年齢，罹患期間，ベースラインでの免疫調節薬の使用及びベースラインでの高感度 C 反応性タンパクとした。各時点での比較は，その時点での投与群間の対比とした。

薬物動態：
各来院時での被験者別のウパダシチニブの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。

安全性：
標準的な安全性解析として，有害事象，特に注目すべき有害事象，臨床検査値及びバイタルサインを評価した。ITT1A 集団及び安全性解析対象集団（SA1A 集団［主要被験者］及び SA1B 集団［追加被験者］）を対象として，安全性についてウパダシチニブ群とプラセボ群間の比較を行った。安全性評価項目は，実際の投与に基づいた投与群ごとに要約した。有害事象については，投与群別に ICH 国際医薬用語集（MedDRA）version 23.0 を用いて発現被験者数及び発現割合を要約した。安全性評価項目の連続変数（臨床検査値及びバイタルサインのベースラインからの変化量等）の投与群間差は，投与群を項とする分散分析モデルを用いて評価し，カテゴリー変数の投与群間差は，Fisher の直接確率検定により評価した。

有効性の結果

主要評価項目では，投与 8 週時の Adapted Mayo スコアによる臨床的寛解率について，複数のウパダシチニブ用量群とプラセボ群の間でおおむね良好な用量反応性が認められ，主要被験者での臨床的寛解率は 45 mg 群（21.4%）で最も高かった（プラセボ群［0%］との比較：$P < 0.001$）。感度分析の結果は，主要解析結果を支持するものであり，M14-234 試験 SS 1 の 30 mg 群及び 45 mg 群にランダム化された追加被験者での結果は，主要被験者の結果と同様であった。

順位付き副次評価項目では，投与 2 週時の部分的 Mayo スコアによる臨床的改善率及び投与 8 週時の内視鏡的寛解率を除き，プラセボ群と比較してすべてのウパダシチニブ群で統計学的有意差が認められた。投与 2 週時の部分的 Mayo スコアによる臨床的改善率及び投与 8 週時の内視

鏡的寛解率では，30 mg 群及び 45 mg 群ではプラセボ群と比較して統計学的有意差が認められたが，ウパダシチニブ 7.5 mg 1 日 1 回群（以下「7.5 mg 群」）及び 15 mg 1 日 1 回群（以下「15 mg 群」）では認められなかった。投与 8 週時の内視鏡的改善率は，プラセボ群で 2.2%であったのに対し，45 mg 群で 35.7%であった。投与 8 週時の Full Mayo スコアによる臨床的寛解率は，プラセボ群で 0%であったのに対し，45 mg 群で 19.6%であった。投与 8 週時の Adapted Mayo スコアによる臨床的改善率及び投与 2 週時の部分的 Mayo スコアによる臨床的改善率は，プラセボ群で 13.0%及び 17.4%であったのに対し，45 mg 群ではいずれも 55.4%であった。M14-234 試験 SS 1 の 30 mg 群及び 45 mg 群にランダム化された追加被験者の結果は，主要被験者の結果と同様であった。

薬物動態の結果

ウパダシチニブの血漿中濃度の平均値は，投与後 24 時間以内では，7.5 mg 群で 2.40–13.3 ng/mL，15 mg 群で 3.60–32.7 ng/mL，30 mg 群で 7.67–59.8 ng/mL，45 mg 群で 10.4–75.4 ng/mL の範囲であった。

安全性の結果

特に記載がない場合は，主要被験者における結果を示す。

- すべての有害事象，重篤な有害事象，高度の有害事象及び治験薬の投与中止に至った有害事象の発現割合は，いずれのウパダシチニブ群でも同程度であり，45 mg 群での治験薬の投与中止に至った有害事象を除き，数値的にプラセボ群の方が高かった。なお，45 mg 群での治験薬の投与中止に至った有害事象の発現割合（8.9%）は，プラセボ群（8.7%）と同程度であった。死亡は，いずれの投与群でも認められなかった。特に注目すべき有害事象のうち，いずれかのウパダシチニブ群で発現割合が 5%超であったものは，薬剤に関連する肝障害，クレアチンホスホキナーゼ増加及び貧血であり，プラセボ群で発現割合が 5%超であったものは，貧血であった。特に注目すべき有害事象のうち，プラセボ群で認められずウパダシチニブ群（特に 45 mg 群）で認められたものは，好中球減少症，リンパ球減少症，クレアチンホスホキナーゼ増加，帯状疱疹及び心血管事象であった。追加被験者におけるすべての有害事象，治験薬と関連ありの有害事象，高度の有害事象，重篤な有害事象及び治験薬の投与中止に至った有害事象を発現した被験者数及び発現割合は，主要被験者の 30 mg 群及び 45 mg 群と一致していた。
- ウパダシチニブ群全体で多く認められた（発現割合が 5%以上）有害事象（基本語）は，頭痛（ウパダシチニブ群全体 8.8%，プラセボ群 10.9%，以下同順）及び潰瘍性大腸炎（6.9%，13.0%）であった。プラセボ群で発現割合が 5%以上であった有害事象は，潰瘍性大腸炎，頭痛，上咽頭炎，偶発的過量投与，貧血及び四肢痛であった。潰瘍性大腸炎の発現割合は，ウパダシチニブ群（いずれの用量群及び全体）と比較してプラセボ群の方が高かった。ウパダシチニブ群全体及びプラセボ群で最も多く認められた治験薬と関連ありの有害事象は，頭痛であった。追加被験者で多く認め

られた（いずれかの投与群で発現割合が 5%以上）有害事象は，上気道感染（6.1%），頭痛（5.3%），ざ瘡（5.3%）及び偶発的過量投与（4.5%）であった。

- 重篤な有害事象の発現割合は，ウパダシチニブ群全体で 3.9%，プラセボ群で 10.9%であった。最も多く認められた重篤な有害事象は，潰瘍性大腸炎であり，発現割合は，ウパダシチニブ群全体で 2.9%，プラセボ群で 4.3%であった。
- 特に注目すべき有害事象のうち，悪性腫瘍，非黒色腫皮膚癌（以下「NMSC」）を除く悪性腫瘍，NMSC，リンパ腫，消化管穿孔，腎機能障害又は活動性結核は，認められなかった。
- 主要被験者の投与 8 週時の血液学的検査のベースラインからの平均変化量（最小二乗平均）について，プラセボ群と比較していずれのウパダシチニブ群でもヘモグロビン量のベースラインからの増加，並びに血小板数及び好中球数のベースラインからの減少が認められた。リンパ球数については，プラセボ群と比較して 7.5 mg 群及び 45 mg 群でベースラインからの増加が認められ，15 mg 群及び 30 mg 群でベースラインからの減少が認められた。主要被験者の投与 8 週時の血液生化学検査のベースラインからの平均変化量について，プラセボ群と比較していずれのウパダシチニブ群でもアラニンアミノトランスフェラーゼ（以下「ALT」），アスパラギン酸アミノトランスフェラーゼ（以下「AST」），クレアチンホスホキナーゼ，クレアチニン及びコレステロールのベースラインからの増加が認められた。
- 主要被験者で Grade 3 以上のヘモグロビン量減少が認められた被験者の割合は，プラセボ群と比較して 7.5 mg 群，15 mg 群及び 30 mg 群の方が高かった。
- Grade 3 以上の好中球数減少が認められた被験者の割合は，プラセボ群と比較して 15 mg 群及び 45 mg 群の方が高かった。Grade 3 以上のリンパ球数減少が認められた被験者の割合は，プラセボ群と比較していずれのウパダシチニブ群でも高かった。Grade 3 以上の ALT 増加又はコレステロール増加は認められなかった。
- Grade 3 の AST 増加は 45 mg 群の 1 例に認められた。Grade 3 以上のクレアチンホスホキナーゼ増加が認められた被験者の割合は，ウパダシチニブ群全体で 3.4%（7 例）であった。
- 収縮期及び拡張期血圧，並びに呼吸数について，投与 8 週時のベースラインからの平均変化量は，いずれのウパダシチニブ群でもプラセボ群と同程度であった。脈拍数については，投与 8 週時にプラセボ群でベースラインから増加したのに対し，7.5 mg 群，15 mg 群及び 45 mg 群でベースラインからの減少が認められ，体重については，プラセボ群と比較していずれのウパダシチニブ群でもベースラインからの増加が認められた。ウパダシチニブ群全体で最も多く認められた臨床的な意義があると判断したバイタルサインは，7%超の体重増加であった（ウパダシチニブ群全体で 8.4%）。

結論

第 IIb 相導入療法用量探索試験である M14-234 試験 SS 1 において，導入療法としてのウパダシチニブ 45 mg 1 日 1 回，8 週間の投与は，主要評価項目の臨床的寛解率でプラセボと比較して

統計学的に有意に高く，すべての順位付き副次評価項目で高い改善効果を示した。また，症状，内視鏡的，組織学的及び生活の質に関する評価項目でも，ウパダシチニブの有効性が示された。

導入療法としてのウパダシチニブ 45 mg 1 日 1 回投与は，おおむね安全で忍容性は良好であった。ウパダシチニブの既知の安全性プロファイルと比較して，新たな安全性のリスクは認められなかった。

本試験の結果は，中等症から重症の活動性 UC 患者を対象とした導入療法として，ウパダシチニブ 45 mg 1 日 1 回投与を裏付けるものであった。これより，第 III 相導入療法試験（M14-234 試験 SS 2 及び M14-675 試験）で使用するウパダシチニブの用量として，45 mg 1 日 1 回を選択した。

日本人部分集団の有害事象

日本人部分集団の有害事象の発現状況を以下に示す。

有害事象の発現割合は，主要被験者ではウパダシチニブ群全体で 57.1%（16/28 例），プラセボ群で 75.0%（3/4 例）であった。2 例以上に認められた有害事象は，ウパダシチニブ群全体では潰瘍性大腸炎及び上咽頭炎であり，プラセボ群では貧血及び潰瘍性大腸炎であった。追加被験者では，有害事象の発現割合は，ウパダシチニブ群全体で 92.3%（12/13 例）であり，2 例以上に認められた有害事象は，白血球減少症，血中クレアチンホスホキナーゼ増加及びざ瘡であった。

治験薬と関連ありの有害事象の発現割合は，主要被験者ではウパダシチニブ群全体で 25.0%（7 例），プラセボ群で 75.0%（3 例）であった。いずれの投与群でも，2 例以上に認められた治験薬と関連ありの有害事象はなかった。追加被験者では，治験薬と関連ありの有害事象の発現割合は，ウパダシチニブ群全体で 38.5%（5 例）であった。

高度の有害事象は，主要被験者ではいずれのウパダシチニブ群でも認められず，プラセボ群で 25.0%（1 例）に認められた。追加被験者では，高度の有害事象の発現割合は，ウパダシチニブ群全体で 7.7%（1 例）であった。

死亡に至った有害事象は，主要被験者及び追加被験者ともに認められなかった。

重篤な有害事象は，主要被験者ではいずれのウパダシチニブ群でも認められず，プラセボ群で 25.0%（1 例）に認められた。追加被験者では，重篤な有害事象の発現割合は，ウパダシチニブ群全体で 7.7%（1 例）であった。

治験薬の投与中止に至った有害事象の発現割合は，主要被験者ではウパダシチニブ群全体で 10.7%（3 例），プラセボ群で 25.0%（1 例）であった。ウパダシチニブ群全体で 2 例以上に認められた治験薬の投与中止に至った有害事象は，潰瘍性大腸炎であった。追加被験者では，治験薬の投与中止に至った有害事象の発現割合は，ウパダシチニブ群全体で 7.7%（1 例）であった。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団	日本人部分集団
有害事象の概要	表 1 (TABLE 14.3__1.1.1_A)	表 8 (TABLE 14.3__1.1.1_A_J)
すべての有害事象	表 2 (TABLE 14.3__1.3.1_A)	表 9 (TABLE 14.3__1.3.1_A_J)
治験薬と関連ありの有害事象	表 3 (TABLE 14.3__1.8_A)	表 10 (TABLE 14.3__1.8_A_J)
高度の有害事象	表 4 (TABLE 14.3__1.9_A)	表 11 (TABLE 14.3__1.9_A_J)
死亡に至った有害事象	表 5 (TABLE 14.3__2.4.9_A)	－（該当被験者なし）
重篤な有害事象	表 6 (TABLE 14.3__2.1.1_A)	表 12 (TABLE 14.3__2.1.1_A_J)
治験薬の投与中止に至った有害事象	表 7 (TABLE 14.3__2.2_A)	表 13 (TABLE 14.3__2.2_A_J)

表1

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.1_A

Overview of Number and Percentage of Subjects with Treatment-Emergent Adverse Events
(Substudy 1 - SA1A Population)

	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
Subjects with:						
Any adverse event (AE)	33 (71.7)	31 (66.0)	31 (63.3)	37 (71.2)	36 (64.3)	135 (66.2)
Any AE with reasonable possibility of being related to study drug$	17 (37.0)	8 (17.0)	13 (26.5)	18 (34.6)	20 (35.7)	59 (28.9)
Any severe AE	7 (15.2)	2 (4.3)	3 (6.1)	3 (5.8)	4 (7.1)	12 (5.9)
Any serious AE	5 (10.9)	0	2 (4.1)	3 (5.8)	3 (5.4)	8 (3.9)
Any AE leading to discontinuation of study drug	4 (8.7)	2 (4.3)	2 (4.1)	4 (7.7)	5 (8.9)	13 (6.4)
Any AE leading to death	0	0	0	0	0	0
Any serious infections	2 (4.3)	0	1 (2.0)	0	2 (3.6)	3 (1.5)
Any opportunistic infections	1 (2.2)	0	0	0	0	0
Any malignancy	0	0	0	0	0	0
Any confirmed malignancy	0	0	0	0	0	0
Any non-melanoma skin cancer (NMSC)	0	0	0	0	0	0
Any confirmed malignancy excluding NMSC	0	0	0	0	0	0
Any lymphoma	0	0	0	0	0	0

Note: Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.
$ As assessed by investigator.
# Includes non treatment-emergent deaths.

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TABLE 14.3 1.1.1 A

Overview of Number and Percentage of Subjects with Treatment-Emergent Adverse Events
(Substudy 1 - SA1A Population)

	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
Any hepatic disorder	1 (2.2)	2 (4.3)	0	0	6 (10.7)	8 (3.9)
Any gastrointestinal perforations	0	0	0	0	0	0
Any anemia	3 (6.5)	1 (2.1)	4 (8.2)	2 (3.8)	0	7 (3.4)
Any neutropenia	0	0	0	0	2 (3.6)	2 (1.0)
Any lymphopenia	0	0	1 (2.0)	1 (1.9)	2 (3.6)	4 (2.0)
Any herpes zoster	0	0	0	0	1 (1.8)	1 (0.5)
Any creatine phosphokinase (CPK) elevation	0	0	3 (6.1)	2 (3.8)	5 (8.9)	10 (4.9)
Any renal dysfunction	0	0	0	0	0	0
Any tuberculosis	0	0	0	0	0	0
Any adjudicated cardiovascular events	0	0	0	0	1 (1.8)	1 (0.5)
Deaths#	0	0	0	0	0	0

Note: Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.
$ As assessed by investigator.
# Includes non treatment-emergent deaths.

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表2

TABLE 14.3__1.3.1_A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
Any adverse event	33 (71.7)	31 (66.0)	31 (63.3)	37 (71.2)	36 (64.3)	135 (66.2)
血液およびリンパ系障害	4 (8.7)	0	3 (6.1)	5 (9.6)	2 (3.6)	10 (4.9)
貧血	3 (6.5)	0	3 (6.1)	1 (1.9)	0	4 (2.0)
好酸球増加症	1 (2.2)	0	0	0	0	0
鉄欠乏性貧血	0	0	0	1 (1.9)	0	1 (0.5)
白血球増加症	0	0	0	1 (1.9)	0	1 (0.5)
白血球減少症	0	0	0	1 (1.9)	0	1 (0.5)
リンパ球減少症	0	0	0	1 (1.9)	1 (1.8)	2 (1.0)
好中球減少症	0	0	0	0	1 (1.8)	1 (0.5)
心臓障害	3 (6.5)	0	1 (2.0)	0	0	1 (0.5)
徐脈	0	0	1 (2.0)	0	0	1 (0.5)
動悸	2 (4.3)	0	0	0	0	0
上室性期外収縮	1 (2.2)	0	0	0	0	0
耳および迷路障害	0	1 (2.1)	0	0	2 (3.6)	3 (1.5)
メニエール病	0	0	0	0	1 (1.8)	1 (0.5)
耳鳴	0	1 (2.1)	0	0	0	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
耳および迷路障害 (Cont.)						
回転性めまい	0	0	0	0	1 (1.8)	1 (0.5)
内分泌障害	0	2 (4.3)	0	0	0	2 (1.0)
クッシング様症状	0	2 (4.3)	0	0	0	2 (1.0)
眼障害	0	2 (4.3)	2 (4.1)	1 (1.9)	1 (1.8)	6 (2.9)
結膜出血	0	1 (2.1)	0	0	0	1 (0.5)
角膜びらん	0	0	1 (2.0)	0	0	1 (0.5)
ドライアイ	0	0	1 (2.0)	0	0	1 (0.5)
眼出血	0	0	0	0	1 (1.8)	1 (0.5)
光視症	0	1 (2.1)	0	0	0	1 (0.5)
硝子体浮遊物	0	0	0	1 (1.9)	0	1 (0.5)
胃腸障害	14 (30.4)	9 (19.1)	9 (18.4)	16 (30.8)	14 (25.0)	48 (23.5)
腹部不快感	1 (2.2)	0	1 (2.0)	0	0	1 (0.5)
腹部膨満	0	3 (6.4)	1 (2.0)	0	1 (1.8)	5 (2.5)
腹痛	1 (2.2)	0	1 (2.0)	1 (1.9)	2 (3.6)	4 (2.0)
下腹部痛	0	0	0	0	1 (1.8)	1 (0.5)
上腹部痛	0	0	1 (2.0)	1 (1.9)	0	2 (1.0)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
胃腸障害 (Cont.)						
腹部圧痛	1 (2.2)	0	0	1 (1.9)	2 (3.6)	3 (1.5)
肛門潰瘍	0	0	0	0	1 (1.8)	1 (0.5)
肛門直腸不快感	0	0	0	0	1 (1.8)	1 (0.5)
大腸炎	1 (2.2)	0	0	0	0	0
潰瘍性大腸炎	6 (13.0)	1 (2.1)	3 (6.1)	6 (11.5)	4 (7.1)	14 (6.9)
便秘	1 (2.2)	0	0	1 (1.9)	0	1 (0.5)
便意切迫	1 (2.2)	0	0	0	0	0
下痢	0	0	0	0	1 (1.8)	1 (0.5)
口内乾燥	0	0	1 (2.0)	0	0	1 (0.5)
排便困難	1 (2.2)	0	0	0	0	0
消化不良	0	0	0	1 (1.9)	0	1 (0.5)
嚥下障害	0	0	0	0	1 (1.8)	1 (0.5)
心窩部不快感	0	0	1 (2.0)	0	0	1 (0.5)
鼓腸	2 (4.3)	2 (4.3)	0	2 (3.8)	0	4 (2.0)
排便回数増加	0	0	1 (2.0)	0	0	1 (0.5)
消化器痛	0	0	1 (2.0)	0	0	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
胃腸障害 (Cont.)						
大腸ポリープ	0	0	1 (2.0)	0	0	1 (0.5)
口腔内潰瘍形成	0	0	0	0	1 (1.8)	1 (0.5)
悪心	2 (4.3)	1 (2.1)	1 (2.0)	6 (11.5)	0	8 (3.9)
食道潰瘍	0	0	0	0	1 (1.8)	1 (0.5)
肛門周囲痛	0	1 (2.1)	0	0	2 (3.6)	3 (1.5)
直腸分泌物	1 (2.2)	0	0	0	0	0
直腸しぶり	0	0	0	0	1 (1.8)	1 (0.5)
口内炎	0	0	0	0	1 (1.8)	1 (0.5)
嘔吐	1 (2.2)	1 (2.1)	1 (2.0)	1 (1.9)	0	3 (1.5)
一般・全身障害および投与部位の状態	7 (15.2)	5 (10.6)	1 (2.0)	11 (21.2)	4 (7.1)	21 (10.3)
無力症	0	1 (2.1)	0	0	0	1 (0.5)
胸部不快感	1 (2.2)	0	0	0	0	0
胸痛	0	0	0	1 (1.9)	0	1 (0.5)
悪寒	1 (2.2)	0	0	2 (3.8)	0	2 (1.0)
疲労	1 (2.2)	2 (4.3)	1 (2.0)	2 (3.8)	1 (1.8)	6 (2.9)
異常感	0	0	0	0	1 (1.8)	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
一般・全身障害および投与部位の状態 (Cont.)						
全身性浮腫	0	0	0	1 (1.9)	0	1 (0.5)
宿酔	1 (2.2)	0	0	0	0	0
インフルエンザ様疾患	1 (2.2)	1 (2.1)	0	1 (1.9)	0	2 (1.0)
倦怠感	0	1 (2.1)	0	0	0	1 (0.5)
腫瘤	0	0	0	0	1 (1.8)	1 (0.5)
疼痛	1 (2.2)	1 (2.1)	0	3 (5.8)	0	4 (2.0)
末梢腫脹	1 (2.2)	0	0	0	0	0
発熱	1 (2.2)	1 (2.1)	0	5 (9.6)	1 (1.8)	7 (3.4)
顔面腫脹	0	1 (2.1)	0	0	0	1 (0.5)
肝胆道系障害	1 (2.2)	0	0	0	1 (1.8)	1 (0.5)
薬物性肝障害	0	0	0	0	1 (1.8)	1 (0.5)
門脈血栓症	1 (2.2)	0	0	0	0	0
免疫系障害	0	0	0	1 (1.9)	0	1 (0.5)
季節性アレルギー	0	0	0	1 (1.9)	0	1 (0.5)
感染症および寄生虫症	16 (34.8)	9 (19.1)	10 (20.4)	9 (17.3)	13 (23.2)	41 (20.1)
膿瘍	1 (2.2)	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
感染症および寄生虫症 (Cont.)						
細菌性膣症	0	0	0	0	1 (1.8)	1 (0.5)
気管支炎	2 (4.3)	0	0	1 (1.9)	0	1 (0.5)
蜂巣炎	1 (2.2)	0	0	0	0	0
クロストリジウム・ディフィシレ感染	1 (2.2)	0	1 (2.0)	0	0	1 (0.5)
膀胱炎	0	1 (2.1)	0	0	0	1 (0.5)
サイトメガロウイルス感染	1 (2.2)	0	0	0	0	0
皮膚糸状菌症	0	1 (2.1)	0	0	0	1 (0.5)
耳感染	0	0	0	1 (1.9)	0	1 (0.5)
毛包炎	1 (2.2)	1 (2.1)	0	1 (1.9)	1 (1.8)	3 (1.5)
胃腸炎	0	1 (2.1)	1 (2.0)	0	0	2 (1.0)
ウイルス性胃腸炎	0	0	0	1 (1.9)	0	1 (0.5)
陰部ヘルペス	0	0	0	1 (1.9)	0	1 (0.5)
歯肉炎	0	0	0	0	1 (1.8)	1 (0.5)
播種性帯状疱疹	0	0	0	0	1 (1.8)	1 (0.5)
麦粒腫	0	0	0	0	1 (1.8)	1 (0.5)
膿痂疹	0	0	0	1 (1.9)	0	1 (0.5)

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Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
感染症および寄生虫症 (Cont.)						
インフルエンザ	0	0	0	1 (1.9)	0	1 (0.5)
限局性感染	1 (2.2)	0	0	0	0	0
下気道感染	1 (2.2)	0	0	0	0	0
ライム病	0	0	0	0	1 (1.8)	1 (0.5)
上咽頭炎	3 (6.5)	1 (2.1)	3 (6.1)	3 (5.8)	3 (5.4)	10 (4.9)
爪真菌症	0	1 (2.1)	0	0	0	1 (0.5)
口腔ヘルペス	1 (2.2)	0	0	0	1 (1.8)	1 (0.5)
中耳炎	0	0	0	0	1 (1.8)	1 (0.5)
咽頭炎	1 (2.2)	0	0	0	0	0
膿疱	0	1 (2.1)	0	0	0	1 (0.5)
RSウイルス感染	0	0	0	0	1 (1.8)	1 (0.5)
鼻炎	1 (2.2)	0	0	0	0	0
敗血症	0	0	0	0	1 (1.8)	1 (0.5)
副鼻腔炎	1 (2.2)	1 (2.1)	0	0	0	1 (0.5)
股部白癬	0	0	0	1 (1.9)	0	1 (0.5)
上気道感染	0	1 (2.1)	4 (8.2)	0	1 (1.8)	6 (2.9)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
感染症および寄生虫症 (Cont.)						
尿路感染	0	1 (2.1)	0	0	0	1 (0.5)
尿路性敗血症	0	0	1 (2.0)	0	0	1 (0.5)
ウイルス感染	1 (2.2)	0	0	0	0	0
ウイルス性咽頭炎	0	0	0	0	1 (1.8)	1 (0.5)
外陰部腟カンジダ症	0	1 (2.1)	0	0	0	1 (0.5)
創傷感染	1 (2.2)	0	0	0	0	0
傷害、中毒および処置合併症	5 (10.9)	2 (4.3)	2 (4.1)	3 (5.8)	4 (7.1)	11 (5.4)
偶発的過量投与	3 (6.5)	0	2 (4.1)	1 (1.9)	1 (1.8)	4 (2.0)
吻合部漏出	1 (2.2)	0	0	0	0	0
挫傷	0	0	0	0	1 (1.8)	1 (0.5)
靭帯捻挫	1 (2.2)	0	0	1 (1.9)	0	1 (0.5)
肉離れ	0	0	0	0	1 (1.8)	1 (0.5)
過量投与	0	1 (2.1)	0	0	0	1 (0.5)
交通事故	0	0	0	1 (1.9)	0	1 (0.5)
皮膚擦過傷	0	0	0	0	1 (1.8)	1 (0.5)
脊椎圧迫骨折	0	1 (2.1)	0	0	0	1 (0.5)

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Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
臨床検査	3 (6.5)	3 (6.4)	6 (12.2)	2 (3.8)	8 (14.3)	19 (9.3)
アラニンアミノトランスフェラーゼ増加	1 (2.2)	2 (4.3)	0	0	0	2 (1.0)
アスパラギン酸アミノトランスフェラーゼ増加	1 (2.2)	2 (4.3)	0	0	3 (5.4)	5 (2.5)
血中アルカリホスファターゼ減少	0	0	0	0	1 (1.8)	1 (0.5)
血中アルカリホスファターゼ増加	1 (2.2)	0	0	0	0	0
血中ビリルビン増加	0	0	0	0	1 (1.8)	1 (0.5)
血中クレアチンホスホキナーゼ増加	0	0	3 (6.1)	2 (3.8)	5 (8.9)	10 (4.9)
血中クレアチニン増加	0	0	0	0	1 (1.8)	1 (0.5)
心電図再分極異常	0	0	1 (2.0)	0	0	1 (0.5)
γ-グルタミルトランスフェラーゼ増加	1 (2.2)	0	0	0	0	0
ヘマトクリット減少	0	0	1 (2.0)	0	0	1 (0.5)
ヘモグロビン減少	0	1 (2.1)	1 (2.0)	0	0	2 (1.0)
肝酵素上昇	0	0	0	0	1 (1.8)	1 (0.5)
リンパ球数減少	0	0	1 (2.0)	0	0	1 (0.5)
リンパ球百分率減少	0	0	0	0	1 (1.8)	1 (0.5)
好中球数減少	0	0	0	0	1 (1.8)	1 (0.5)

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Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
臨床検査 (Cont.)						
好中球数増加	0	0	1 (2.0)	0	1 (1.8)	2 (1.0)
尿中蛋白陽性	1 (2.2)	0	0	0	0	0
赤血球数減少	0	0	1 (2.0)	0	0	1 (0.5)
体重減少	1 (2.2)	0	0	0	0	0
白血球数減少	0	0	1 (2.0)	0	0	1 (0.5)
白血球数増加	0	0	1 (2.0)	0	1 (1.8)	2 (1.0)
代謝および栄養障害	6 (13.0)	3 (6.4)	3 (6.1)	3 (5.8)	1 (1.8)	10 (4.9)
食欲減退	2 (4.3)	0	1 (2.0)	0	0	1 (0.5)
糖尿病性代謝代償不全	0	0	1 (2.0)	0	0	1 (0.5)
体液貯留	0	1 (2.1)	0	0	0	1 (0.5)
高血糖	1 (2.2)	1 (2.1)	1 (2.0)	0	1 (1.8)	3 (1.5)
高脂血症	1 (2.2)	0	0	0	0	0
低カリウム血症	0	1 (2.1)	0	1 (1.9)	0	2 (1.0)
低マグネシウム血症	0	0	0	1 (1.9)	0	1 (0.5)
低リン酸血症	2 (4.3)	0	0	2 (3.8)	0	2 (1.0)
鉄欠乏	1 (2.2)	0	0	0	0	0

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program source code: [redacted]

TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
筋骨格系および結合組織障害	8 (17.4)	4 (8.5)	5 (10.2)	4 (7.7)	4 (7.1)	17 (8.3)
関節痛	1 (2.2)	2 (4.3)	0	1 (1.9)	0	3 (1.5)
関節障害	0	1 (2.1)	0	1 (1.9)	1 (1.8)	3 (1.5)
背部痛	1 (2.2)	0	0	1 (1.9)	0	1 (0.5)
滑液包炎	0	0	1 (2.0)	0	0	1 (0.5)
側腹部痛	1 (2.2)	0	0	0	0	0
椎間板突出	0	0	1 (2.0)	0	0	1 (0.5)
関節腫脹	1 (2.2)	0	0	0	0	0
筋不快感	1 (2.2)	0	0	0	0	0
筋痙縮	1 (2.2)	0	1 (2.0)	1 (1.9)	0	2 (1.0)
筋骨格系胸痛	0	0	1 (2.0)	0	0	1 (0.5)
筋骨格痛	1 (2.2)	0	0	0	0	0
筋骨格硬直	0	0	0	0	1 (1.8)	1 (0.5)
骨粗鬆症	0	1 (2.1)	0	0	1 (1.8)	2 (1.0)
四肢痛	3 (6.5)	0	0	0	1 (1.8)	1 (0.5)
多発性関節炎	1 (2.2)	0	0	0	0	0

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program source code: [redacted]

TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
筋骨格系および結合組織障害 (Cont.)						
脊椎関節障害	0	0	1 (2.0)	0	0	1 (0.5)
顎関節症候群	0	0	0	0	1 (1.8)	1 (0.5)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)	0	1 (2.1)	0	0	0	1 (0.5)
メラノサイト性母斑	0	1 (2.1)	0	0	0	1 (0.5)
神経系障害	6 (13.0)	7 (14.9)	5 (10.2)	6 (11.5)	6 (10.7)	24 (11.8)
注意力障害	0	1 (2.1)	0	0	0	1 (0.5)
浮動性めまい	1 (2.2)	1 (2.1)	0	1 (1.9)	0	2 (1.0)
頭痛	5 (10.9)	4 (8.5)	4 (8.2)	5 (9.6)	5 (8.9)	18 (8.8)
神経痛	0	0	0	0	1 (1.8)	1 (0.5)
橈骨神経麻痺	0	0	0	1 (1.9)	0	1 (0.5)
緊張性頭痛	1 (2.2)	0	0	0	0	0
振戦	0	1 (2.1)	1 (2.0)	0	0	2 (1.0)
精神障害	2 (4.3)	3 (6.4)	1 (2.0)	3 (5.8)	2 (3.6)	9 (4.4)
感情障害	0	0	0	0	1 (1.8)	1 (0.5)
激越	0	1 (2.1)	0	0	0	1 (0.5)
不安	1 (2.2)	0	1 (2.0)	1 (1.9)	0	2 (1.0)

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Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
精神障害 (Cont.)						
うつ病	0	1 (2.1)	0	0	0	1 (0.5)
初期不眠症	0	0	0	1 (1.9)	0	1 (0.5)
不眠症	1 (2.2)	1 (2.1)	1 (2.0)	1 (1.9)	1 (1.8)	4 (2.0)
腎および尿路障害	1 (2.2)	2 (4.3)	0	0	2 (3.6)	4 (2.0)
膀胱痛	1 (2.2)	0	0	0	0	0
腎結石症	0	0	0	0	1 (1.8)	1 (0.5)
頻尿	1 (2.2)	1 (2.1)	0	0	1 (1.8)	2 (1.0)
腎臓痛	0	1 (2.1)	0	0	0	1 (0.5)
生殖系および乳房障害	0	1 (2.1)	0	0	0	1 (0.5)
外陰膣痛	0	1 (2.1)	0	0	0	1 (0.5)
呼吸器、胸郭および縦隔障害	2 (4.3)	3 (6.4)	2 (4.1)	5 (9.6)	2 (3.6)	12 (5.9)
咳嗽	1 (2.2)	1 (2.1)	1 (2.0)	2 (3.8)	1 (1.8)	5 (2.5)
呼吸困難	0	0	0	2 (3.8)	0	2 (1.0)
口腔咽頭痛	0	1 (2.1)	2 (4.1)	2 (3.8)	0	5 (2.5)
副鼻腔分泌過多	0	1 (2.1)	0	0	0	1 (0.5)
気胸	1 (2.2)	0	0	0	0	0

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Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)						
肺塞栓症	0	0	0	0	1 (1.8)	1 (0.5)
鼻漏	0	0	0	1 (1.9)	0	1 (0.5)
低音性連続性ラ音	0	0	0	0	1 (1.8)	1 (0.5)
皮膚および皮下組織障害	2 (4.3)	3 (6.4)	2 (4.1)	12 (23.1)	6 (10.7)	23 (11.3)
ざ瘡	0	1 (2.1)	1 (2.0)	4 (7.7)	1 (1.8)	7 (3.4)
脱毛症	0	0	1 (2.0)	1 (1.9)	1 (1.8)	3 (1.5)
ざ瘡様皮膚炎	0	0	0	1 (1.9)	0	1 (0.5)
接触皮膚炎	1 (2.2)	0	0	0	0	0
斑状出血	0	0	0	0	1 (1.8)	1 (0.5)
紅斑	0	0	0	1 (1.9)	0	1 (0.5)
寝汗	0	1 (2.1)	0	0	0	1 (0.5)
皮膚疼痛	0	0	0	0	1 (1.8)	1 (0.5)
そう痒症	1 (2.2)	0	0	0	0	0
発疹	0	1 (2.1)	0	3 (5.8)	1 (1.8)	5 (2.5)
毛孔性皮疹	0	0	0	0	1 (1.8)	1 (0.5)
そう痒性皮疹	0	0	0	1 (1.9)	0	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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TABLE 14.3 1.3.1 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
皮膚および皮下組織障害 (Cont.)						
酒さ	0	0	0	1 (1.9)	0	1 (0.5)
皮膚亀裂	0	0	0	0	1 (1.8)	1 (0.5)
血管障害	1 (2.2)	2 (4.3)	2 (4.1)	0	1 (1.8)	5 (2.5)
深部静脈血栓症	0	0	0	0	1 (1.8)	1 (0.5)
潮紅	0	1 (2.1)	1 (2.0)	0	0	2 (1.0)
血腫	0	1 (2.1)	0	0	0	1 (0.5)
高血圧	0	0	1 (2.0)	0	0	1 (0.5)
低血圧	1 (2.2)	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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表3

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL

TABLE 14.3__1.8_A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
Any adverse event	17 (37.0)	8 (17.0)	13 (26.5)	18 (34.6)	20 (35.7)	59 (28.9)
血液およびリンパ系障害	2 (4.3)	0	0	2 (3.8)	2 (3.6)	4 (2.0)
貧血	1 (2.2)	0	0	1 (1.9)	0	1 (0.5)
好酸球増加症	1 (2.2)	0	0	0	0	0
白血球減少症	0	0	0	1 (1.9)	0	1 (0.5)
リンパ球減少症	0	0	0	0	1 (1.8)	1 (0.5)
好中球減少症	0	0	0	0	1 (1.8)	1 (0.5)
眼障害	0	0	0	1 (1.9)	0	1 (0.5)
硝子体浮遊物	0	0	0	1 (1.9)	0	1 (0.5)
胃腸障害	4 (8.7)	1 (2.1)	2 (4.1)	6 (11.5)	4 (7.1)	13 (6.4)
腹部不快感	0	0	1 (2.0)	0	0	1 (0.5)
腹部膨満	0	0	0	0	1 (1.8)	1 (0.5)
腹痛	1 (2.2)	0	1 (2.0)	0	1 (1.8)	2 (1.0)
上腹部痛	0	0	0	1 (1.9)	0	1 (0.5)
肛門潰瘍	0	0	0	0	1 (1.8)	1 (0.5)
肛門直腸不快感	0	0	0	0	1 (1.8)	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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TABLE 14.3 1.8 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
胃腸障害 (Cont.)						
大腸炎	1 (2.2)	0	0	0	0	0
潰瘍性大腸炎	1 (2.2)	0	0	0	2 (3.6)	2 (1.0)
口内乾燥	0	0	1 (2.0)	0	0	1 (0.5)
鼓腸	1 (2.2)	1 (2.1)	0	2 (3.8)	0	3 (1.5)
排便回数増加	0	0	1 (2.0)	0	0	1 (0.5)
悪心	0	0	0	4 (7.7)	0	4 (2.0)
肛門周囲痛	0	0	0	0	1 (1.8)	1 (0.5)
直腸分泌物	1 (2.2)	0	0	0	0	0
直腸しぶり	0	0	0	0	1 (1.8)	1 (0.5)
一般・全身障害および投与部位の状態	0	1 (2.1)	0	2 (3.8)	4 (7.1)	7 (3.4)
悪寒	0	0	0	1 (1.9)	0	1 (0.5)
疲労	0	0	0	1 (1.9)	1 (1.8)	2 (1.0)
異常感	0	0	0	0	1 (1.8)	1 (0.5)
腫瘤	0	0	0	0	1 (1.8)	1 (0.5)
発熱	0	0	0	1 (1.9)	1 (1.8)	2 (1.0)
顔面腫脹	0	1 (2.1)	0	0	0	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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TABLE 14.3 1.8 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
感染症および寄生虫症	4 (8.7)	2 (4.3)	2 (4.1)	3 (5.8)	5 (8.9)	12 (5.9)
膿瘍	1 (2.2)	0	0	0	0	0
蜂巣炎	1 (2.2)	0	0	0	0	0
クロストリジウム・ディフィシレ感染	1 (2.2)	0	0	0	0	0
皮膚糸状菌症	0	1 (2.1)	0	0	0	1 (0.5)
毛包炎	0	0	0	1 (1.9)	1 (1.8)	2 (1.0)
陰部ヘルペス	0	0	0	1 (1.9)	0	1 (0.5)
播種性帯状疱疹	0	0	0	0	1 (1.8)	1 (0.5)
膿痂疹	0	0	0	1 (1.9)	0	1 (0.5)
口腔ヘルペス	0	0	0	0	1 (1.8)	1 (0.5)
咽頭炎	1 (2.2)	0	0	0	0	0
RSウイルス感染	0	0	0	0	1 (1.8)	1 (0.5)
敗血症	0	0	0	0	1 (1.8)	1 (0.5)
上気道感染	0	1 (2.1)	1 (2.0)	0	1 (1.8)	3 (1.5)
尿路性敗血症	0	0	1 (2.0)	0	0	1 (0.5)
創傷感染	1 (2.2)	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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TABLE 14.3 1.8 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
傷害、中毒および処置合併症	3 (6.5)	1 (2.1)	2 (4.1)	1 (1.9)	1 (1.8)	5 (2.5)
偶発的過量投与	3 (6.5)	0	2 (4.1)	1 (1.9)	1 (1.8)	4 (2.0)
過量投与	0	1 (2.1)	0	0	0	1 (0.5)
臨床検査	1 (2.2)	1 (2.1)	5 (10.2)	0	3 (5.4)	9 (4.4)
アラニンアミノトランスフェラーゼ増加	1 (2.2)	1 (2.1)	0	0	0	1 (0.5)
アスパラギン酸アミノトランスフェラーゼ増加	1 (2.2)	1 (2.1)	0	0	1 (1.8)	2 (1.0)
血中アルカリホスファターゼ増加	1 (2.2)	0	0	0	0	0
血中クレアチンホスホキナーゼ増加	0	0	3 (6.1)	0	1 (1.8)	4 (2.0)
心電図再分極異常	0	0	1 (2.0)	0	0	1 (0.5)
γ-グルタミルトランスフェラーゼ増加	1 (2.2)	0	0	0	0	0
リンパ球百分率減少	0	0	0	0	1 (1.8)	1 (0.5)
好中球数減少	0	0	0	0	1 (1.8)	1 (0.5)
白血球数減少	0	0	1 (2.0)	0	0	1 (0.5)
代謝および栄養障害	1 (2.2)	0	1 (2.0)	0	0	1 (0.5)
食欲減退	0	0	1 (2.0)	0	0	1 (0.5)
低リン酸血症	1 (2.2)	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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TABLE 14.3 1.8 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
筋骨格系および結合組織障害	1 (2.2)	1 (2.1)	0	2 (3.8)	2 (3.6)	5 (2.5)
関節痛	0	1 (2.1)	0	1 (1.9)	0	2 (1.0)
筋痙縮	1 (2.2)	0	0	1 (1.9)	0	1 (0.5)
筋骨格硬直	0	0	0	0	1 (1.8)	1 (0.5)
四肢痛	0	0	0	0	1 (1.8)	1 (0.5)
顎関節症候群	0	0	0	0	1 (1.8)	1 (0.5)
神経系障害	4 (8.7)	0	3 (6.1)	3 (5.8)	3 (5.4)	9 (4.4)
浮動性めまい	0	0	0	1 (1.9)	0	1 (0.5)
頭痛	4 (8.7)	0	3 (6.1)	2 (3.8)	3 (5.4)	8 (3.9)
精神障害	1 (2.2)	0	0	1 (1.9)	0	1 (0.5)
不眠症	1 (2.2)	0	0	1 (1.9)	0	1 (0.5)
腎および尿路障害	0	2 (4.3)	0	0	1 (1.8)	3 (1.5)
頻尿	0	1 (2.1)	0	0	1 (1.8)	2 (1.0)
腎臓痛	0	1 (2.1)	0	0	0	1 (0.5)
呼吸器、胸郭および縦隔障害	0	0	1 (2.0)	1 (1.9)	1 (1.8)	3 (1.5)
咳嗽	0	0	1 (2.0)	0	0	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.8 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)						
口腔咽頭痛	0	0	0	1 (1.9)	0	1 (0.5)
肺塞栓症	0	0	0	0	1 (1.8)	1 (0.5)
皮膚および皮下組織障害	1 (2.2)	1 (2.1)	1 (2.0)	3 (5.8)	2 (3.6)	7 (3.4)
ざ瘡	0	1 (2.1)	0	0	0	1 (0.5)
脱毛症	0	0	1 (2.0)	1 (1.9)	0	2 (1.0)
皮膚疼痛	0	0	0	0	1 (1.8)	1 (0.5)
そう痒症	1 (2.2)	0	0	0	0	0
発疹	0	0	0	2 (3.8)	0	2 (1.0)
毛孔性皮疹	0	0	0	0	1 (1.8)	1 (0.5)
血管障害	0	1 (2.1)	0	0	1 (1.8)	2 (1.0)
深部静脈血栓症	0	0	0	0	1 (1.8)	1 (0.5)
血腫	0	1 (2.1)	0	0	0	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

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表4

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__1.9_A

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
Any adverse event	7 (15.2)	2 (4.3)	3 (6.1)	3 (5.8)	4 (7.1)	12 (5.9)
血液およびリンパ系障害	0	0	1 (2.0)	0	0	1 (0.5)
貧血	0	0	1 (2.0)	0	0	1 (0.5)
胃腸障害	4 (8.7)	0	1 (2.0)	2 (3.8)	2 (3.6)	5 (2.5)
肛門潰瘍	0	0	0	0	1 (1.8)	1 (0.5)
大腸炎	1 (2.2)	0	0	0	0	0
潰瘍性大腸炎	2 (4.3)	0	1 (2.0)	2 (3.8)	1 (1.8)	4 (2.0)
排便困難	1 (2.2)	0	0	0	0	0
一般・全身障害および投与部位の状態	0	1 (2.1)	0	1 (1.9)	0	2 (1.0)
悪寒	0	0	0	1 (1.9)	0	1 (0.5)
発熱	0	1 (2.1)	0	1 (1.9)	0	2 (1.0)
感染症および寄生虫症	2 (4.3)	0	1 (2.0)	0	1 (1.8)	2 (1.0)
蜂巣炎	1 (2.2)	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.9 A

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
感染症および寄生虫症 (Cont.)						
RSウイルス感染	0	0	0	0	1 (1.8)	1 (0.5)
敗血症	0	0	0	0	1 (1.8)	1 (0.5)
副鼻腔炎	1 (2.2)	0	0	0	0	0
尿路性敗血症	0	0	1 (2.0)	0	0	1 (0.5)
臨床検査	0	1 (2.1)	1 (2.0)	0	0	2 (1.0)
血中クレアチンホスホキナーゼ増加	0	0	1 (2.0)	0	0	1 (0.5)
ヘモグロビン減少	0	1 (2.1)	0	0	0	1 (0.5)
代謝および栄養障害	1 (2.2)	0	0	0	0	0
低リン酸血症	1 (2.2)	0	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0	0	1 (1.8)	1 (0.5)
肺塞栓症	0	0	0	0	1 (1.8)	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

表5

[redacted]20[redacted] 10:50 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__2.4.9_A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Death
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A and SA1B Population)

		ABT-494				
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	7.5 mg QD (N=47) n (%)	15 mg QD (N=49) n (%)	30 mg QD (N=52) n (%)	45 mg QD (N=56) n (%)	Total (N=204) n (%)
Any adverse event	0	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 2.4.9 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Death
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A and SA1B Population)

MedDRA 23.0 System Organ Class Preferred Term	ABT-494 30 mg QD (N=65) n (%)	ABT-494 45 mg QD (N=67) n (%)	Total (N=132) n (%)
Any adverse event	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

表6

[redacted]20[redacted] 10:50 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__2.1.1_A

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
Any adverse event	5 (10.9)	0	2 (4.1)	3 (5.8)	3 (5.4)	8 (3.9)
胃腸障害	2 (4.3)	0	1 (2.0)	3 (5.8)	2 (3.6)	6 (2.9)
潰瘍性大腸炎	2 (4.3)	0	1 (2.0)	3 (5.8)	2 (3.6)	6 (2.9)
感染症および寄生虫症	2 (4.3)	0	1 (2.0)	0	2 (3.6)	3 (1.5)
蜂巣炎	1 (2.2)	0	0	0	0	0
RSウイルス感染	0	0	0	0	1 (1.8)	1 (0.5)
敗血症	0	0	0	0	1 (1.8)	1 (0.5)
副鼻腔炎	1 (2.2)	0	0	0	0	0
尿路性敗血症	0	0	1 (2.0)	0	0	1 (0.5)
ウイルス性咽頭炎	0	0	0	0	1 (1.8)	1 (0.5)
臨床検査	0	0	0	0	1 (1.8)	1 (0.5)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	0	1 (1.8)	1 (0.5)
代謝および栄養障害	1 (2.2)	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 2.1.1 A

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
代謝および栄養障害 (Cont.)						
低リン酸血症	1 (2.2)	0	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0	0	1 (1.8)	1 (0.5)
肺塞栓症	0	0	0	0	1 (1.8)	1 (0.5)
血管障害	0	0	0	0	1 (1.8)	1 (0.5)
深部静脈血栓症	0	0	0	0	1 (1.8)	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

表7

[redacted]20[redacted] 10:50 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__2.2_A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
Any adverse event	4 (8.7)	2 (4.3)	2 (4.1)	4 (7.7)	5 (8.9)	13 (6.4)
血液およびリンパ系障害	0	0	0	0	1 (1.8)	1 (0.5)
リンパ球減少症	0	0	0	0	1 (1.8)	1 (0.5)
胃腸障害	3 (6.5)	0	2 (4.1)	4 (7.7)	3 (5.4)	9 (4.4)
上腹部痛	0	0	0	1 (1.9)	0	1 (0.5)
肛門潰瘍	0	0	0	0	1 (1.8)	1 (0.5)
大腸炎	1 (2.2)	0	0	0	0	0
潰瘍性大腸炎	2 (4.3)	0	2 (4.1)	3 (5.8)	2 (3.6)	7 (3.4)
悪心	0	0	0	1 (1.9)	0	1 (0.5)
一般・全身障害および投与部位の状態	0	0	0	1 (1.9)	0	1 (0.5)
悪寒	0	0	0	1 (1.9)	0	1 (0.5)
発熱	0	0	0	1 (1.9)	0	1 (0.5)
感染症および寄生虫症	0	0	0	0	1 (1.8)	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 2.2 A

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=46) n (%)	ABT-494 7.5 mg QD (N=47) n (%)	ABT-494 15 mg QD (N=49) n (%)	ABT-494 30 mg QD (N=52) n (%)	ABT-494 45 mg QD (N=56) n (%)	ABT-494 Total (N=204) n (%)
感染症および寄生虫症 (Cont.)						
ウイルス性咽頭炎	0	0	0	0	1 (1.8)	1 (0.5)
臨床検査	0	1 (2.1)	0	0	1 (1.8)	2 (1.0)
アラニンアミノトランスフェラーゼ増加	0	1 (2.1)	0	0	0	1 (0.5)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (2.1)	0	0	0	1 (0.5)
好中球数減少	0	0	0	0	1 (1.8)	1 (0.5)
代謝および栄養障害	1 (2.2)	0	0	0	0	0
低リン酸血症	1 (2.2)	0	0	0	0	0
神経系障害	0	1 (2.1)	0	0	0	1 (0.5)
頭痛	0	1 (2.1)	0	0	0	1 (0.5)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

表8

[redacted]20[redacted] 09:39 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__1.1.1_A_J

Overview of Number and Percentage of Subjects with Treatment-Emergent Adverse Events
(Substudy 1 - SA1A Population Japan Analysis Set)

		ABT-494				
	Placebo (N=4) n (%)	7.5 mg QD (N=4) n (%)	15 mg QD (N=5) n (%)	30 mg QD (N=9) n (%)	45 mg QD (N=10) n (%)	Total (N=28) n (%)
Subjects with:						
Any adverse event (AE)	3 (75.0)	1 (25.0)	2 (40.0)	6 (66.7)	7 (70.0)	16 (57.1)
Any AE with reasonable possibility of being related to study drug$	3 (75.0)	0	1 (20.0)	3 (33.3)	3 (30.0)	7 (25.0)
Any severe AE	1 (25.0)	0	0	0	0	0
Any serious AE	1 (25.0)	0	0	0	0	0
Any AE leading to discontinuation of study drug	1 (25.0)	1 (25.0)	0	1 (11.1)	1 (10.0)	3 (10.7)
Any AE leading to death	0	0	0	0	0	0
Any serious infections	0	0	0	0	0	0
Any opportunistic infections	0	0	0	0	0	0
Any malignancy	0	0	0	0	0	0
Any confirmed malignancy	0	0	0	0	0	0
Any non-melanoma skin cancer (NMSC)	0	0	0	0	0	0
Any confirmed malignancy excluding NMSC	0	0	0	0	0	0
Any lymphoma	0	0	0	0	0	0

Note: Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.
$ As assessed by investigator.
# Includes non treatment-emergent deaths.

program source code: [redacted]

TABLE 14.3 1.1.1 A J

Overview of Number and Percentage of Subjects with Treatment-Emergent Adverse Events
(Substudy 1 - SA1A Population Japan Analysis Set)

	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
Any hepatic disorder	1 (25.0)	0	0	0	1 (10.0)	1 (3.6)
Any gastrointestinal perforations	0	0	0	0	0	0
Any anemia	2 (50.0)	0	0	1 (11.1)	0	1 (3.6)
Any neutropenia	0	0	0	0	1 (10.0)	1 (3.6)
Any lymphopenia	0	0	0	0	1 (10.0)	1 (3.6)
Any herpes zoster	0	0	0	0	0	0
Any creatine phosphokinase (CPK) elevation	0	0	0	0	0	0
Any renal dysfunction	0	0	0	0	0	0
Any tuberculosis	0	0	0	0	0	0
Any adjudicated cardiovascular events	0	0	0	0	0	0
Deaths#	0	0	0	0	0	0

Note: Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.
$ As assessed by investigator.
# Includes non treatment-emergent deaths.

program source code: [redacted]

表9

[redacted]20[redacted] 10:23 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 4

TABLE 14.3__1.3.1_A_J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
Any adverse event	3 (75.0)	1 (25.0)	2 (40.0)	6 (66.7)	7 (70.0)	16 (57.1)
血液およびリンパ系障害	2 (50.0)	0	0	2 (22.2)	1 (10.0)	3 (10.7)
貧血	2 (50.0)	0	0	1 (11.1)	0	1 (3.6)
白血球減少症	0	0	0	1 (11.1)	0	1 (3.6)
好中球減少症	0	0	0	0	1 (10.0)	1 (3.6)
耳および迷路障害	0	0	0	0	2 (20.0)	2 (7.1)
メニエール病	0	0	0	0	1 (10.0)	1 (3.6)
回転性めまい	0	0	0	0	1 (10.0)	1 (3.6)
胃腸障害	2 (50.0)	0	0	2 (22.2)	3 (30.0)	5 (17.9)
潰瘍性大腸炎	2 (50.0)	0	0	1 (11.1)	1 (10.0)	2 (7.1)
下痢	0	0	0	0	1 (10.0)	1 (3.6)
悪心	0	0	0	1 (11.1)	0	1 (3.6)
口内炎	0	0	0	0	1 (10.0)	1 (3.6)
一般・全身障害および投与部位の状態	0	0	0	1 (11.1)	0	1 (3.6)
発熱	0	0	0	1 (11.1)	0	1 (3.6)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
肝胆道系障害	1 (25.0)	0	0	0	1 (10.0)	1 (3.6)
薬物性肝障害	0	0	0	0	1 (10.0)	1 (3.6)
門脈血栓症	1 (25.0)	0	0	0	0	0
感染症および寄生虫症	1 (25.0)	0	0	1 (11.1)	3 (30.0)	4 (14.3)
膿瘍	1 (25.0)	0	0	0	0	0
毛包炎	0	0	0	1 (11.1)	0	1 (3.6)
ウイルス性胃腸炎	0	0	0	1 (11.1)	0	1 (3.6)
歯肉炎	0	0	0	0	1 (10.0)	1 (3.6)
麦粒腫	0	0	0	0	1 (10.0)	1 (3.6)
上咽頭炎	0	0	0	0	2 (20.0)	2 (7.1)
創傷感染	1 (25.0)	0	0	0	0	0
傷害、中毒および処置合併症	1 (25.0)	0	0	1 (11.1)	0	1 (3.6)
吻合部漏出	1 (25.0)	0	0	0	0	0
靱帯捻挫	0	0	0	1 (11.1)	0	1 (3.6)
臨床検査	2 (50.0)	0	1 (20.0)	0	1 (10.0)	2 (7.1)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
臨床検査 (Cont.)						
アラニンアミノトランスフェラーゼ増加	1 (25.0)	0	0	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (25.0)	0	0	0	0	0
血中アルカリホスファターゼ増加	1 (25.0)	0	0	0	0	0
γ-グルタミルトランスフェラーゼ増加	1 (25.0)	0	0	0	0	0
リンパ球百分率減少	0	0	0	0	1 (10.0)	1 (3.6)
尿中蛋白陽性	1 (25.0)	0	0	0	0	0
白血球数減少	0	0	1 (20.0)	0	0	1 (3.6)
筋骨格系および結合組織障害	0	0	1 (20.0)	0	0	1 (3.6)
椎間板突出	0	0	1 (20.0)	0	0	1 (3.6)
神経系障害	0	1 (25.0)	0	0	1 (10.0)	2 (7.1)
頭痛	0	1 (25.0)	0	0	0	1 (3.6)
神経痛	0	0	0	0	1 (10.0)	1 (3.6)
呼吸器、胸郭および縦隔障害	1 (25.0)	0	0	0	0	0
気胸	1 (25.0)	0	0	0	0	0
皮膚および皮下組織障害	0	0	0	1 (11.1)	1 (10.0)	2 (7.1)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.3.1 A J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
皮膚および皮下組織障害 (Cont.)						
ざ瘡様皮膚炎	0	0	0	1 (11.1)	0	1 (3.6)
皮膚疼痛	0	0	0	0	1 (10.0)	1 (3.6)
血管障害	1 (25.0)	0	0	0	0	0
低血圧	1 (25.0)	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

表10

[redacted]20[redacted] 10:23 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__1.8_A_J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
Any adverse event	3 (75.0)	0	1 (20.0)	3 (33.3)	3 (30.0)	7 (25.0)
血液およびリンパ系障害	1 (25.0)	0	0	2 (22.2)	1 (10.0)	3 (10.7)
貧血	1 (25.0)	0	0	1 (11.1)	0	1 (3.6)
白血球減少症	0	0	0	1 (11.1)	0	1 (3.6)
好中球減少症	0	0	0	0	1 (10.0)	1 (3.6)
胃腸障害	1 (25.0)	0	0	0	0	0
潰瘍性大腸炎	1 (25.0)	0	0	0	0	0
感染症および寄生虫症	1 (25.0)	0	0	1 (11.1)	0	1 (3.6)
膿瘍	1 (25.0)	0	0	0	0	0
毛包炎	0	0	0	1 (11.1)	0	1 (3.6)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

TABLE 14.3 1.8 A J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
with Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
感染症および寄生虫症 (Cont.)						
創傷感染	1 (25.0)	0	0	0	0	0
臨床検査	1 (25.0)	0	1 (20.0)	0	1 (10.0)	2 (7.1)
アラニンアミノトランスフェラーゼ増加	1 (25.0)	0	0	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (25.0)	0	0	0	0	0
血中アルカリホスファターゼ増加	1 (25.0)	0	0	0	0	0
γ-グルタミルトランスフェラーゼ増加	1 (25.0)	0	0	0	0	0
リンパ球百分率減少	0	0	0	0	1 (10.0)	1 (3.6)
白血球数減少	0	0	1 (20.0)	0	0	1 (3.6)
皮膚および皮下組織障害	0	0	0	0	1 (10.0)	1 (3.6)
皮膚疼痛	0	0	0	0	1 (10.0)	1 (3.6)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

表11

[redacted]20[redacted] 10:23 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__1.9_A_J

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
Any adverse event	1 (25.0)	0	0	0	0	0
胃腸障害	1 (25.0)	0	0	0	0	0
潰瘍性大腸炎	1 (25.0)	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

表12

[redacted]20[redacted] 10:23 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.1.1_A_J

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
Any adverse event	1 (25.0)	0	0	0	0	0
胃腸障害	1 (25.0)	0	0	0	0	0
潰瘍性大腸炎	1 (25.0)	0	0	0	0	0

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

表13

[redacted]20[redacted] 10:23 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.2_A_J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(Substudy 1 - SA1A Population Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=4) n (%)	ABT-494 7.5 mg QD (N=4) n (%)	ABT-494 15 mg QD (N=5) n (%)	ABT-494 30 mg QD (N=9) n (%)	ABT-494 45 mg QD (N=10) n (%)	ABT-494 Total (N=28) n (%)
Any adverse event	1 (25.0)	1 (25.0)	0	1 (11.1)	1 (10.0)	3 (10.7)
胃腸障害	1 (25.0)	0	0	1 (11.1)	1 (10.0)	2 (7.1)
潰瘍性大腸炎	1 (25.0)	0	0	1 (11.1)	1 (10.0)	2 (7.1)
神経系障害	0	1 (25.0)	0	0	0	1 (3.6)
頭痛	0	1 (25.0)	0	0	0	1 (3.6)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent AEs during Substudy 1 are defined as events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and within 30 days after the last dose of the study medication in Substudy 1 for subjects who discontinued Substudy 1 and are not enrolled into Substudy 3 or study M14-533, or events that begin or worsen either on or after the first dose of the study medication in Substudy 1 and up to the first dose of the study medication in Substudy 3 or study M14-533.

program source code: [redacted]

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

Reason [redacted]

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

Treatment Group	Age at Study Start	Sex	Race
Placebo	5[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
EYE DISEASE/DISORDER: BILATERAL SEROSA CENTRALIS	20[redacted]
EYE DISEASE/DISORDER: BLEPHARITIS	20[redacted]
EYE DISEASE/DISORDER: GLAUCOMA	NOT REPORTED
HEPATITIS: AZATHIOPRINE INDUCED HEPATITIS	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ARTHRALGIA KNEES	20[redacted]
OTHER: FOLIC ACID DEPLETION	20[redacted]
OTHER: INTERMITTENT ARTHRALGIA	20[redacted]
OTHER: TIREDNESS	NOT REPORTED
OTHER: TRIGEMINAL NEURALGIA	19[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.15 PACK	24	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted]
PARACETAMOL	1 g	PRN	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
GOLIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
BLINDED THERAPY	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
ETROLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BECLOMETASONE	10 mg	QD	Y-M: 20[redacted] / -360
BLINDED THERAPY	NOT REPORTED	OTHER: 1/4WEEKS	Y-M: 20[redacted] / -282
INVESTIGATIONAL DRUG	600.000 mg	OTHER: 1/4WEEKS	Y-M: 20[redacted] / -192
INVESTIGATIONAL DRUG	200.000 mg	OTHER: 1/4WEEKS	Y-M: 20[redacted] / -102
SPIRONOLACTONE	50 mg	QD	Y-M: 20[redacted] / -95
FOLIC ACID	0.4 mg	QD	Y-M: 20[redacted] / -76
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -76
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -14
PYRIDOXINE	250 mg	EVERY WEEK	Y-M: 20[redacted] / -14
MIDAZOLAM	4 mg	QD	Y-M: 20[redacted] / -4
PETHIDINE	50 mg	QD	Y-M: 20[redacted] / -4
AZATHIOPRINE	150 mg	QD	Y: 20[redacted]
MESALAZINE	NOT REPORTED	QD	Y: 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
PARACETAMOL	1 g	PRN	Y-M: 20[redacted]	ONGOING
MESALAZINE	2 g	BID	Y-M: 20[redacted]	ONGOING
SPIRONOLACTONE	50 mg	QD	Y-M: 20[redacted] / -95	Y-M: 20[redacted] / 42

FOLIC ACID	0.4 mg	QD	Y-M: 20[redacted] / -76	Y-M: 20[redacted] / 41
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -76	ONGOING
PARACETAMOL	1 g	QD	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 41
AMOXICILLIN;CLAVULANIC ACID	1 g	TID	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 33
IRON	1 g	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 35
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 37
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 46
PIPERACILLIN;TAZOBACTAM	4 g	OTHER: 4/DAY	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 48
SODIUM CHLORIDE;WATER	100 mL	PRN	Y-M: 20[redacted] / 41	ONGOING
IRON	1 g	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 42	ONGOING
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 48
ZOLPIDEM	5 mg	PRN	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 50
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 46	ONGOING
ACETYLSALICYLIC ACID	80 mg	QD	Y-M: 20[redacted] / 47	ONGOING
IOMEPROL	100 mL	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 47

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

Event Description WORSENING SINUSITIS

Preferred term 副鼻腔炎

AE Onset Date / Rx Day [redacted]20[redacted] / 41

Age at AE Onset 5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 41): Leukocytes: 16.98 [4 - 10] 10^9/L; NPTST159-CRP: 109.4 [NOT REPORTED - 5] mg/L; Neutrophils: 13.7 [2.5 - 7.8] 10^9/L; [redacted]20[redacted] (RX DAY 43): NPTST159-CRP: 97.5 [NOT REPORTED - 5] mg/L; [redacted]20[redacted] (RX DAY 46): Leukocytes: 14.13 [4 - 10] 10^9/L; NPTST159-CRP: 78.3 [NOT REPORTED - 5] mg/L; [redacted]20[redacted] (RX DAY 48): Leukocytes: 11.69 [4 - 10] 10^9/L; NPTST159-CRP: 61.5 [NOT REPORTED - 5] mg/L

Microbiology

[redacted]20[redacted] (RX DAY 41): STOOL NPTST121-CLOSTRIDIUM DIFFICILE DETECTION: NEGATIVE; SPUTUM NPTST164-CULTURE: POSITIVE-CITROBACTER FREUNDII; URINE NPTST164-CULTURE: NEGATIVE; STOOL NPTST164-CULTURE: NEGATIVE; BLOOD NPTST251-HAEMOCULTURE: NEGATIVE; STOOL NPTST374-PARASITOLOGY: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 41): ABDOMINAL ULTRA SOUND: COLITIS DESCENDENS + SIGMOIDITIS; CT SINUSES: PANSINUSITIS; ECG: SINUS TACHYCARDIA; RX THORAX: NORMAL; [redacted]20[redacted] (RX DAY 47): CT SINUSSES: INFLAMMATORY CHANGES RHINOSINUSAL, MOSTLY IN THE LEFT SINUS MAXILLARIS

AE Stopped Rx Day 48

Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はベルギーの成人男性であり，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，グレード 3 の副鼻腔炎の悪化の事象を発現した。関連する病歴は，元喫煙者（1 日 0.15 箱を 24 年間）であった。

Event 1 の臨床経過：

投与21日後＊，被験者は副鼻腔炎（非重篤，継続中）を発現した。

投与41日後＊　，被験者は副鼻腔炎の悪化を発現した。投与48日後＊　　，副鼻腔炎の悪化は消失した。

投与41日後＊　　，被験者は，頭痛，発熱，白色痰を伴う咳嗽，三叉神経痛，鼻汁及び鼻水の徴候及び症状があり，入院した。投与48日後＊，被験者は退院した。

投与された薬剤は，tradonal，paracetamol，stilnoct，イオメロン 350，tavanic，ピペラシリン・タゾバクタム合剤，injectafer，asaflow，imodium 及び sterimar であった。

The patient's past medications include:

ANTI IL-23 for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

---

1) Sinusitis (10040753) (Sinusitis (10040753)) [v.20.0] [10040753]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of WORSENING SINUSITIS

- Investigator: Unknown.

- AbbVie: Event related to worsening of prior condition.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 109.4 MG/L (normal <5)

[redacted] **20[redacted] CRP:** 97.5 MG/L (normal <5)

[redacted] **20[redacted] CRP:** 61.5 MG/L

[redacted] **20[redacted] CT SINUSES:** Pansinusitis

[redacted] **20[redacted] CT SINUSES:** Inflammatory changes rhinosinusal, mostly in the left sinus maxillaris.

[redacted] **20[redacted] HEMOCULTURE:** Negative

[redacted] **20[redacted] NEUTROPHILS ABSOLUTE:** 13.7 X10**9/L (normal 2.5 to 7.8)

[redacted] **20[redacted] SPUTUM CULTURE:** Positive: Citrobacter Freundii

[redacted] **20[redacted] STOOL CLOSTRIDIUM DIFFICILE DETECTION:** Negative

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

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

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

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

[redacted] **20[redacted] WHITE BLOOD CELLS:** 16.98 X10**9/L (normal 4.00 to 10.00)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 14.13 X10**9/L

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.69 X10**9/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
アスパラギン酸アミノトランスフェラーゼ増加	X			X
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 45 mg	2[redacted]	MALE	WHITE

Medical History	Onset Year
LEFT SIDED UC	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45	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
MESALAZINE	4 g	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	TID	Y-M: 20[redacted]

CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	BID	Y-M: 20[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]
PREDNISONE	1 mg	QD	Y-M: 20[redacted] / -328
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -245
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -203

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -245	Not reported
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 33
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1000 mL	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 38
DROTAVERINE	80 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 38
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 38
RANITIDINE	150 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 38
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 45
PREDNISOLONE	20 mg	BID	Y-M: 20[redacted] / 37	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Hepatic disorder

Event Description AST INCREASED

Preferred term アスパラギン酸アミノトランスフェラーゼ増加

AE Onset Date / Rx Day [redacted]20[redacted] / 30

Age at AE Onset 2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 34): NPTST438-S,P-CRP: 154.0 [1 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	34
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ONE TIME ALCHOHOL USE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 32
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 34): Alanine Aminotransferase: 54 [5 - 55] U/L; Aspartate Aminotransferase: 40 [5 - 34] U/L; Hemoglobin: 115 [130 - 170] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	38
Duration of AE	7 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	HOSPITALIZATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:25
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はエストニアの 2[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，潰瘍性大腸炎及び AST 増加の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び禁酒であった。

Event 1 及び 2 の臨床経過：

投与30日後＊ ，被験者は発熱（非重篤）を発現した。投与30日後＊ ，被験者は AST 増加を発現した。投与32日後＊ ，被験者は潰瘍性大腸炎を発現した。投与34日後＊ ，AST 増加は消失した。投与38日後＊，潰瘍性大腸炎は消失した。

投与32日後＊ ，被験者は下痢，腹痛及び発熱があり，潰瘍性大腸炎の悪化と診断されて入院した。発熱（非重篤）は 投与33日後＊ に消失した。被験者は 投与38日後＊ に退院した。入院中の被験者の事象の経過について，その他の詳細は提供されなかった。

投与された薬剤は，cerucal，paracetamol，prednisolon，metronidazol，ラクトリンゲル，ranitidin 及び no spa であった。

The patient's past medications include:

MESALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], Started [redacted] 20[redacted])

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

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

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

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

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

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

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

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

Causality for ABT-494 (Blinded)

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1) Ulcerative colitis (10045365) (Colitis ulcerative (10009900)) [v.20.1] [10045365]

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

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

Dechallenge: No

2) AST increased (10003544) (Aspartate aminotransferase increased (10003481)) [v.20.1] [10003544]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

Event of ULCERATIVE COLITIS

- Investigator: Hospitalization.

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

Event of AST INCREASED

- Investigator: One time alcohol use.

- AbbVie: Event is more likely related to the ulcerative colitis flare diagnosed 2 days after onset of the event.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 54.0 U/L (normal 5.0 to 55.0)

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 40 U/L (normal 5.0 to 34.0)

[redacted] **20[redacted] CRP:** 154.0 mg/L (normal 1.0 to 5.0)

[redacted] **20[redacted] HEMOGLOBIN:** 115 G/L (normal 130 to 170)

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
低リン酸血症	X	X		

Treatment Group	Age at Study Start	Sex	Race
Placebo	2[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: ANEMIA DUE TO ACTIVE COLITIS	20[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO ASPARTAME	NOT REPORTED
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: LACTOSE INTOLERANCE	NOT REPORTED

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CALCIUM CARBONATE;COLECALCIFEROL	500/400 OTHER: MG/IU	PRN	Y-M: 20[redacted]
MESALAZINE	3200 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	60 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	60 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
BENACTYZINE;METAMIZOLE;PITOFENONE	500/5 mg	PRN	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	60 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METHYLPREDNISOLONE	60 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	BID	Y-M: 20[redacted]
IRON	1000.000 mg	OTHER: ONE INFUSION	Y-M: 20[redacted]
METHYLPREDNISOLONE	60 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PHENOXYMETHYLPENICILLIN	1500 IU	TID	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
IRON	1000.000 mg	OTHER: ONE INFUSION	Y-M: 20[redacted]
IRON	1000.000 mg	OTHER: ONE INFUSION	Y-M: 20[redacted]
CEFALEXIN	500 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -190
CEFALEXIN	500 mg	TID	Y-M: 20[redacted] / -208
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -93
TRAMADOL	50.000 mg	PRN	Y-M: 20[redacted] / -93

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CALCIUM CARBONATE;COLECALCIFEROL	500/400 OTHER: MG/IU	PRN	Y-M: 20[redacted]	ONGOING
MESALAZINE	3200 mg	BID	Y-M: 20[redacted]	ONGOING
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]	ONGOING
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 20	ONGOING
IRON	1000 mg	OTHER: ONE TIME INFUSION	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 32
SODIUM GLYCEROPHOSPHATE	1 mmol	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 46
COLECALCIFEROL	100 ug	QD	Y-M: 20[redacted] / 46	ONGOING
COLECALCIFEROL	300 000 IU	OTHER: ONE TIME INJECTION	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 46
COLECALCIFEROL	100 000 IU	OTHER: ONE TIME INJECTION	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 64
SODIUM GLYCEROPHOSPHATE	1 mmol	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 67
ALFACALCIDOL	25 ug	OTHER: 1+2	Y-M: 20[redacted] / 68	ONGOING
SODIUM PHOSPHATE MONOBASIC (ANHYDROUS)	500 mg	TID	Y-M: 20[redacted] / 68	ONGOING

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

Event Description HYPOPHOSPHATEMIA

Preferred term 低リン酸血症

AE Onset Date / Rx Day [redacted]20[redacted] / 41

Age at AE Onset 2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 43): Calcium: 1.26 [1 - 1.5] MMOL/L; Hemoglobin: 105 [134 - 1667] G/L; Leukocytes: 8.7 [3.4 - 8.2] 10^9/L; NPTST159-CRP: 11 [NOT REPORTED - 10] mg/L; NPTST367-P-MG: 0.74 [0.71 - 0.94] MMOL/L; Phosphate: 0.2 [0.71 - 1.53] MMOL/L; Platelets: 593 [150 - 360] 10^9/L; Potassium: 4 [3.3 - 4.9] MMOL/L; Sodium: 140 [137 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 44): Phosphate: 0.3 [0.71 - 1.53] MMOL/L; [redacted]20[redacted] (RX DAY 45): Alanine Aminotransferase: 9 [10 - 70] U/L; Alkaline Phosphatase: 74 [35 - 105] U/L; Creatine Kinase: 43 [50 - 400] U/L; NPTST224-FP-GLUC: 4.5 [4 - 7] MMOL/L; NPTST225-FP-PTH-INT: 57 [10 - 60] NG/L; NPTST364-P-D-25: 21 [50 - NOT REPORTED] NMOL/L; NPTST367-P-MG: 0.87 [0.71 - 0.94] MMOL/L; Phosphate: 0.3 [0.71 - 1.53] MMOL/L; [redacted]20[redacted] (RX DAY 46): NPTST446-SEDIMENTATION RATE: 33 [0 - 15] MM/H; Phosphate: 0.4 [0.71 - 1.53] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 43): EKG: NORMAL

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

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はフィンランドの 2[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，低リン酸血症の事象を発現した。関連する病歴は，広範囲な潰瘍性大腸炎（全大腸炎型），活動性大腸炎による貧血，非喫煙者及び少量の現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与41日後＊，被験者は低リン酸血症を発現した。

投与41日後＊　　，定期受診時の臨床検査の結果，リン酸塩値が低値（0.37 mmol/L）であった。被験者には低リン酸血症の症状はなかった。投与43日後＊　　，被験者はリン酸塩値が 0.2 mmol/L となり，入院した。入院時，身体検査に異常はなく，心電図も正常であった。被験者は，リン酸塩の静脈内投与を 3 日間受けた。リン酸塩値は 0.4 mmol/L まで上昇した。リン酸塩を多く含む食事が推奨された。また，ビタミン D 注射剤及び経口ビタミン D サプリメントの投与が開始された。投与46日後＊，被験者は退院した。

投与された薬剤は，d3vicotrat，ビタミン D3，glycophos，etalpha，vitamin d3 streuli 及び phosphate sandoz であった。

Causality for ABT-494 (Blinded)

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1) Hypophosphatemia (10021059) (Hypophosphataemia (10021058)) [v.20.1] [10021059]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of HYPOPHOSPHATEMIA

- Investigator: Not applicable.

- AbbVie: Event is more likely related to decreased intestinal absorption from pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 9 No units (normal 20 to 70)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 74 U/L (normal 35 to 105)

[redacted] **20[redacted] CALCIUM:** 1.26 MMOL/L (normal 1 to 1.5)

[redacted] **20[redacted] CREATINE KINEASE:** 43 U/L (normal 50 to 400)

[redacted] **20[redacted] CRP:** 11 MG/L (normal <10)

[redacted] **20[redacted] D25-VITAMIN:** 21 nmol/l (normal >50)

[redacted] **20[redacted] EKG:** Normal

[redacted] **20[redacted] FASTING GLUCOSE:** Unknown

[redacted] **20[redacted] HEMOGLOBIN:** 105 G/L (normal 134 to 1667)

[redacted] **20[redacted] INORGANIC PHOSPORUS:** 0.2 MMOL/L (normal 0.71 to 1.53)

[redacted] **20[redacted] INORGANIC PHOSPORUS:** 0.3 MMOL/L (normal 0.71 to 1.53)

[redacted] **20[redacted] INORGANIC PHOSPORUS:** 0.3 MMOL/L (normal 0.71 to 1.53)

[redacted] **20[redacted] INORGANIC PHOSPORUS:** 0.4 MMOL/L (normal 0.71 to 1.53)

[redacted] **20[redacted] PHOSPHATE:** 0.37 MMOL/L

[redacted] **20[redacted] PLATELET COUNT:** 593 X10**9/L (normal 150 to 360)

[redacted] **20[redacted] POTASSIUM:** 4.0 MMOL/L (normal 3.3 to 4.9)

[redacted] **20[redacted] PTH:** 57 NG/L (normal 10 to 60)

[redacted] **20[redacted] SEDIMENTATION RATE:** 33 MM/HR (normal 0 to 15)

[redacted] **20[redacted] SODIUM:** 140 MMOL/L (normal 137 to 145)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.7 X10**9/L (normal 3.4 to 8.2)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
アラニンアミノトランスフェラーゼ増加				X
貧血				X
アスパラギン酸アミノトランスフェラーゼ増加				X
潰瘍性大腸炎	X	X		
γ-グルタミルトランスフェラーゼ増加				X

Treatment Group	Age at Study Start	Sex	Race
Placebo	3[redacted]	FEMALE	ASIAN

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: PERIPHERAL ARTHROPATHY	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.5 PACK	10	
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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 30	30

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
BETAMETHASONE	1 mg	PRN	Y-M: 20[redacted]
BETAMETHASONE	3 mg	PRN	Y-M: 20[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	125 mg	QD	Y-M: 20[redacted] / -187
VONOPRAZAN	10 mg	QD	Y-M: 20[redacted] / -126
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -73
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PAC	OTHER: ONCE	Y-M: 20[redacted] / -26
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	OTHER: ONCE	Y-M: 20[redacted] / -26
DIMETICONE	20 mL	OTHER: ONCE	Y-M: 20[redacted] / -26
FLUMAZENIL	0.5 mg	OTHER: ONCE	Y-M: 20[redacted] / -26
GLUCOSE	100 mL	OTHER: ONCE	Y-M: 20[redacted] / -26
HYOSCINE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / -26
MIDAZOLAM	3 mg	OTHER: ONCE	Y-M: 20[redacted] / -26
NALOXONE	0.2 mg	OTHER: ONCE	Y-M: 20[redacted] / -26
PETHIDINE	35 mg	OTHER: ONCE	Y-M: 20[redacted] / -26

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]	Not reported
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]	Not reported

PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 31
BETAMETHASONE	1 mg	PRN	Y-M: 20[redacted]	Not reported
AZATHIOPRINE	125 mg	QD	Y-M: 20[redacted] / -187	Y-M: 20[redacted] / -12
VONOPRAZAN	10 mg	QD	Y-M: 20[redacted] / -126	Y-M: 20[redacted] / 31
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -73	Y-M: 20[redacted] / 31
LOXOPROFEN	50 mg	PRN	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 31
PIPERACILLIN;TAZOBACTAM	4.5 g	BID	Y-M: 20[redacted] / 39	Y-M: 20[redacted] / 39
DOPAMINE	200-500 OTHER: MG/DAY	PRN	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 50
PIPERACILLIN;TAZOBACTAM	4.5 g	TID	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 40
AMIKACIN	100 mg	BID	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 49
PIPERACILLIN;TAZOBACTAM	4.5 g	QID	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 49
HEPARIN	10000-20000 OTHER: UNIT/DAY	PRN	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 51

Event #1: Event of Interest - Hepatic disorder

Event Description	GGT INCREASED, ALP INCREASED, ALT INCREASED, AST,INCREASED
Preferred term	アラニンアミノトランスフェラーゼ増加，アスパラギン酸アミノトランスフェラーゼ増加，γ-グルタミルトランスフェラーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 18
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	37 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	20 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	WORSENING OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 31 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 31): CT: WORSENING OF UC; [redacted]20[redacted] (RX DAY 32): OPERATION: CONDUCTED TOTAL PROCTOCOLECTOMY WITH ILEOSTOMY AND IPAA AND RECOVERED FROM WORSENUNG OF UC; [redacted]20[redacted] (RX DAY 39): CT: PORTAL VEIN THROMBUS	
AE Stopped Rx Day	59 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	29 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INADEQUATE RESPONSE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 32 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	57 (27 DAYS AFTER LAST TREATMENT)
Duration of AE	26 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE

Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:25
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，現喫煙者（1 日 0.5 箱を 10 年間）及び元飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与18日後＊，被験者は肝酵素上昇（非重篤，継続中）を発現した。

投与31日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与59日後＊　　，潰瘍性大腸炎の悪化は消失した。

被験者は投与31日後＊　　に潰瘍性大腸炎の悪化のため，入院した。徴候及び症状は，摂氏 39.0°C–39.9°C の発熱及び腹痛であった。投与32日後＊　，回腸瘻造設及び IPAA（回腸嚢肛門吻合術）を伴う直腸結腸全切除術を受けた。術後，吻合部漏出（非重篤，投与39日後＊–投与50日後＊）　　，門脈血栓症（非重篤，投与39日後＊–投与51日後＊）　　，気胸（非重篤，投与40日後＊–投与43日後＊）　，膿瘍形成（非重篤，投与39日後＊）　　，貧血（非重篤，投与32日後＊–投与57日後＊）　　，創傷感染（非重篤，投与39日後＊–投与59日後＊）　及び低血圧（非重篤，投与40日後＊–投与51日後＊）　　を発現した。投与59日後＊，被験者は回復し，退院した。

投与された薬剤は，イノバン，ヘパリンナトリウム，タゾピペ及びアミカシン硫酸塩であった。

The patient's past medications include:

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

IMURAN for ULCERATIVE COLITIS (Started [redacted] 20[redacted])

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

RINDERON for ULCERATIVE COLITIS (Started [redacted] 20[redacted])

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

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

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

Causality for ABT-494 (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of WORSENING OF UC

- Investigator: Inadequate response

- AbbVie: Event is clearly consistent with progression or worsening of the underlying disease and is considered expected for this study.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] COLONOSCOPY:** 20 - distance of demarcation from the anal verge; 3 endoscopy subscore

[redacted] **20[redacted] CT:** worsening of uc

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Alanine aminotransferase increased:Asymptomatic.
Aspartate aminotransferase increased:Asymptomatic.
Gamma-glutamyltranferase increased:Asymptomatic.

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ABT-494 45 mg	4[redacted]	MALE	ASIAN

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	19[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: EPIGASTRIC PAIN	20[redacted]
HEPATITIS: HEPATITIS B	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	5	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 14	14

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]-[redacted]

BETAMETHASONE	NOT REPORTED	OTHER: UNKNOWN	Y-M: 20[redacted]
OTHER THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: LCAP WAS CONDUCTED FIVE TIMES BETWEEN [redacted] 20[redacted] AND [redacted] 20[redacted].	Y-M: 20[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	45 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	75 mg	QD	Y-M: 20[redacted]
MESALAZINE	3600 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted] / -341
CLOSTRIDIUM BUTYRICUM	20 mg	TID	Y-M: 20[redacted] / -316
VONOPRAZAN	10 mg	QD	Y-M: 20[redacted] / -316
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -252
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -273
MESALAZINE	1 g	QD	Y-M: 20[redacted] / -228
OTHER THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: 2 TIME PER WEEK	Y-M: 20[redacted] / -235
TACROLIMUS	5 mg	BID	Y-M: 20[redacted] / -238
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / -242
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -210
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	OTHER: ONCE	Y-M: 20[redacted] / -12
DIMETICONE	20 mL	OTHER: ONCE	Y-M: 20[redacted] / -12
HYOSCINE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / -12
MIDAZOLAM	4 mg	OTHER: ONCE	Y-M: 20[redacted] / -12
PETHIDINE	35 mg	OTHER: ONCE	Y-M: 20[redacted] / -12
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / -13
MESALAZINE	2000 mg	BID	Y: 19[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
MESALAZINE	3600 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 15

AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / -341 / -11
CLOSTRIDIUM BUTYRICUM	20 mg	TID	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / -316 / 15
VONOPRAZAN	10 mg	QD	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / -316 / 15
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / -12 / -12
DIMETICONE	20 mL	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / -12 / -12
HYOSCINE	20 mg	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / -12 / -12
MIDAZOLAM	4 mg	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / -12 / -12
PETHIDINE	35 mg	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / -12 / -12
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / -13 / -13
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 13 / 14
CEFMETAZOLE	1 g	BID	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 17
DROPERIDOL	2 mL	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 18
FENTANYL	0.3 mg	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 15
FENTANYL	1 mg	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 18
HYDROXYZINE	50 mg	PRN	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 15
LEVOBUPIVACAINE	200 mL	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 18
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 18
PROPOFOL	28 mg	PRN	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 15
REMIFENTANIL	5 mg	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 15
ROCURONIUM	40 mg	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 15
ROPIVACAINE	33 mL	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted] [redacted] / 15 / 15

HALOPERIDOL	5 mg	PRN	Y-M: 20[redacted]- [redacted] / 16	Y-M: 20[redacted]- / 16
HYDROXYZINE	50 mg	PRN	Y-M: 20[redacted]- [redacted] / 17	Y-M: 20[redacted]- / 17
PIPERACILLIN;TAZOBACTAM	4.5 g	BID	Y-M: 20[redacted]- [redacted] / 17	ONGOING

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

Event Description	UC AGGRAVATED
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 13
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 14): Albumin: 29 [41 - 51] G/L

Microbiology

[redacted]20[redacted] (RX DAY 13): STOOL NPTST084-C.DIFFICILE ANTIGEN AND TOXINS: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 13): ABDOMINAL CT SCAN: IDENTIFIED AN EXACERBATION OF THE UC; [redacted]20[redacted] (RX DAY 15): OPERATION: CONDUCTED LAPAROSCOPIC LARGE INTESTINE COMPLETE REMOVAL AND RECOVERED FROM WORSENING OF UC

AE Stopped Rx Day	26 (12 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC AGGRAVATED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 5 年間），潰瘍性大腸炎及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与13日後＊　　，被験者は潰瘍性大腸炎の悪化を発現した。投与26日後＊　　，潰瘍性大腸炎の悪化は消失した。

投与5日後＊　　，被験者は発熱した。投与5日後＊から 投与11日後＊の間，体温は摂氏37.0°C–37.5°C であった。投与13日後＊　　，被験者は血便の増加が認められた。投与13日後＊，被験者は発熱，腹痛及び血便があり，入院した。投与15日後＊　，被験者は回腸嚢肛門吻合術を伴う腹腔鏡下直腸結腸全切除術を受けた。投与26日後＊，被験者は退院した。

投与された薬剤は，セフメタゾール，タゾピペ及びアセリオであった。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

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

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

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

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

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

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

CELLSORBA-EX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1)　UC aggravated (10045283)　(Colitis ulcerative (10009900))　[v.21.0]　[10045283]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of UC AGGRAVATED

- Investigator: UC aggravated.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL CT SCAN:** Identified an exacerbation of the UC

[redacted] **ALBUMIN:** 2.9 G/DL (normal 4.1 to 5.1)

[redacted] **BODY TEMPERATURE:** 39.4 Degrees C

[redacted] **BODY TEMPERATURE:** 38.0 Degrees C

[redacted] **C.DIFFICILE ANTIGEN AND TOXINS:** 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
貧血				X
潰瘍性大腸炎	X			
イレウス	X			

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

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	19[redacted]
LEFT SIDED UC	19[redacted]
OSTEOPOROSIS: OSTEOPENIA LUMBAR SPINE	20[redacted]
OTHER: ANAL FISSURE	20[redacted]
OTHER: FIBULA FRACTURE RIGHT SIDE	20[redacted]
OTHER: GENERAL PAIN	20[redacted]
OTHER: HYPERHYDROSIS OF THE ARMPITS AND FEET	19[redacted]
OTHER: INTERMITTENT JOINT PAINS FROM OVEREXERTION	20[redacted]
OTHER: LIVER FUNCTION ABNORMALITIES	20[redacted]
OTHER: SUSPICION OF INFECTION OCAMPYLOBACTER AND YERSINA INFECTION	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 30 mg	30	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BUDESONIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METHOTREXATE	25 mg	OTHER: ONCE PER WEEK	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
BUDESONIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MERCAPTOPURINE	100 mg	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	2400 mg	QD	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METHOTREXATE	15 mg	OTHER: ONCE PER WEEK	Y-M: 20[redacted]
METHOTREXATE	10 mg	OTHER: ONCE PER WEEK	Y-M: 20[redacted]
MESALAZINE	66.7 mg	QD	Y-M: 20[redacted]
METHOTREXATE	25 mg	OTHER: ONCE PER WEEK	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
SULFAMETHOXAZOLE;TRIMETHOPRIM	800 mg	OTHER: 3 X PER WEEK	Y-M: 20[redacted]
HYDROCORTISONE	200 mg	OTHER: TOGETHER WITH INFLIXIMAB	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BUDESONIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	OTHER: ONCE PER WEEK	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted]

LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted]
MESALAZINE	66.7 mg	QD	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
BUDESONIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BUDESONIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -364
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -322
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -334
METHOTREXATE	25 mg	OTHER: ONCE PER WEEK	Y-M: 20[redacted] / -313
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -282
SULFAMETHOXAZOLE;TRIMETHOPRIM	400 mg	OTHER: 1 X PER MONTH	Y-M: 20[redacted] / -282
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / -220
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -221
URSODEOXYCHOLIC ACID	500 mg	BID	Y-M: 20[redacted] / -221
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -221
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -140
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -112
CALCIUM;VITAMIN D NOS	1000/800 OTHER: MG/IU	QD	Y-M: 20[redacted] / -74
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / -12
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -24
AZATHIOPRINE	200 mg	QD	Y: 20[redacted]
BETAMETHASONE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
HYDROCORTISONE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y: 20[redacted]
BUDESONIDE	9 mg	NOT REPORTED	Y: 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
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 83
URSODEOXYCHOLIC ACID	500 mg	BID	Y-M: 20[redacted] / -221	Y-M: 20[redacted] / 58
CALCIUM;VITAMIN D NOS	1000/800 OTHER: MG/IU	QD	Y-M: 20[redacted] / -74	ONGOING
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / -12	ONGOING
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -24	Y-M: 20[redacted] / 57

IRON	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 32
LIDOCAINE	UK OTHER: UK	PRN	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 50
NADROPARIN	2850 IU	QD	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 60
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 60
SODIUM CHLORIDE	2 OTHER: L	OTHER: /24H	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 83
TEMAZEPAM	10 mg	PRN	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 83
CEFAZOLIN	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 54
CLONIDINE	37.5 ug	OTHER: ONCE	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 54
HYDROCORTISONE	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 54
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 57
METRONIDAZOLE	2000 mg	OTHER: ONCE	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 54
MORPHINE	2 mg	PRN	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 54
MORPHINE	500 OTHER: MG/250ML	OTHER: 0.25ML/H	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 57
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 83
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 83
HYDROCORTISONE	DAY 1 100 DAY 2 75 DAY 3 50 mg	QD	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 57
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 67
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 81
MORPHINE	5 mg	PRN	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 80
NADROPARIN	2850 IU	QD	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 80
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 71
SODIUM CHLORIDE	2 OTHER: L	OTHER: /24H	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 79
SODIUM CITRATE;SODIUM LAURYL SULFOACETATE	625 OTHER: MG/ML	BID	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 70
AMIDOTRIZOIC ACID	UNK OTHER: N/A	OTHER: ONCE	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 71
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 80
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 83
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 81

SODIUM PHOSPHATE;SODIUM PHOSPHATE MONOBASIC (ANHYDROUS)	UNK OTHER: N/A	OTHER: N/A	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 70
ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE;SIMETICONE	15 mL	TID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 73
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 95
RICINUS COMMUNIS	15 mL	BID	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 73
LACTULOSE	15 mL	BID	Y-M: 20[redacted] / 73	Y-M: 20[redacted] / 77
RICINUS COMMUNIS	1 mL	QD	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 78
AMIDOTRIZOIC ACID	UNK OTHER: NA	QD	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 79
NITROFURANTOIN	50 mg	OTHER: FOUR TIMES A DAY	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 86
BETAMETHASONE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]	Not reported
HYDROCORTISONE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]	Not reported
AZATHIOPRINE	150 mg	QD	Y: 20[redacted]	Not reported

Event #1: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 31
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	32
Duration of AE	2 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	EXACERBATION UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 47 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 50): Aspartate Aminotransferase: 18 [0 - 35] U/L; Creatinine: 88 [64 - 104] UMOL/L; Hemoglobin: 130.51854 [136.9639 - 161.134] G/L; Potassium: 4.1 [3.5 - 5.1] MMOL/L; Sodium: 142 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 51): NPTST208-FECAL CALPROTECTIN: 1633 [0 - 50] ?G/G; [redacted]20[redacted] (RX DAY 57): Erythrocytes: 22 [0 - 18] UNIT NOT REPORTED; Leukocytes: >900 [0 - 10] UNIT NOT REPORTED; NPTST049-BACTERIA: 220-750 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 59): Aspartate Aminotransferase: 32 [0 - 35] U/L; [redacted]20[redacted] (RX DAY 60): Hemoglobin: 122.46184 [136.9639 - 177.2474] G/L

Microbiology

[redacted]20[redacted] (RX DAY 51): STOOL NPTST055-BACTERIOLOGY AND VIROLOGY: NEGATIVE-NO ORGANISMS IDENTIFIED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 50): ABDOMINAL X-RAY: NO SIGNS OF TOXIC MEGACOLON; [redacted]20[redacted] (RX DAY 54): SUBTOTAL COLECTOMY: SUCCESFUL

AE Stopped Rx Day	60 (16 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	EXACERBATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #3: Serious Adverse Event

Event Description	ILEUS
Preferred term	イレウス
AE Onset Date / Rx Day	[redacted]20[redacted] / 66 (22 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 66): Hemoglobin: 132.12988 [136.9639 - 177.2474] G/L; Leukocytes: 32 [0 - 10] UNIT NOT REPORTED; Leukocytes: 17.21 [4 - 10] 10^9/L; [redacted]20[redacted] (RX DAY 72): Erythrocytes: 29 [0 - 18] UNIT NOT REPORTED; Hemoglobin: 133.74122 [136.9639 - 177.2474] G/L; Leukocytes: 67 [0 - 10] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	81 (37 DAYS AFTER LAST TREATMENT)
Duration of AE	16 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	STOMA STENOSIS LEADING TO ILEUS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:10:25
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はオランダの 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，イレウス及び潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 2 及び 3 の臨床経過：

投与47日後＊ ，被験者は潰瘍性大腸炎の悪化を発現した。投与60日後＊ ，潰瘍性大腸炎の悪化は消失した。投与66日後＊，被験者はイレウスを発現した。

投与47日後＊ ，被験者は頻回な排便，腹痛及び出血の症状を以前より多く発現した。投与50日後＊ ，1 日 13–15 回の頻回な排便及び疲労があり，入院した。投与51日後＊ ，便の回数が 1 日 20 回に増え，被験者は腹痛の増加を発現した。投与54日後＊ ，結腸亜全摘術を受け，成功した。投与57日後＊ ，被験者は排尿時の痛み，尿路感染を発現した。投与60日後＊，被験者は退院した。

投与66日後＊ ，被験者は激しい腹痛で救急治療室を受診した。被験者は激しい痛みを感じた。同日，被験者は入院した。ストーマに狭窄が認められた。被験者は複数回の浣腸剤の投与を受けた。投与67日後＊ ，被験者は頭痛を発現し，paracetamol を投与された。投与69日後＊，腹痛を発現した。入院中，被験者はイレウスのために腹部 CT スキャン検査，血液学的検査

及び尿検査を受けた。投与75日後＊，被験者は退院した。

投与77日後＊　　，被験者は再入院した。投与81日後＊　，被験者は退院した。投与81日後＊，イレウスは消失した。

投与された薬剤は，塩化ナトリウム，オキシコドン，paracetamol，prednisolon，microlax，リン酸塩注腸剤，モルヒネ，オキノーム，wonder oil，ラクツロース，ブデソニド注腸剤，antagel 及び pantoprazol であった。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS (20[redacted] - 20[redacted], Started 20[redacted])

BETHESOL for ULCERATIVE COLITIS (Started 20[redacted])

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

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

HYDROCORTISON for ULCERATIVE COLITIS and ULCERATIVE COLITIS (Started 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

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

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

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

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

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

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

Causality for ABT-494 (Blinded)

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1) Ileus (10021328) (Ileus (10021328)) [v.21.0] [10021328]

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

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

Dechallenge: Not Applicable

2) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.21.0] [10045283]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of ILEUS

- Investigator: STOMA STENOSIS LEADING TO ILEUS.

- AbbVie: EVENT MORE LIKELY A COMPLICATION OF PRIOR COLECTOMY.

Event of EXACERBATION UC

- Investigator: EXACERBATION

- AbbVie: EVENT MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

Unknown date ABDOMINAL CT: Unknown

[redacted] **20[redacted] ABDOMINAL X-RAY:** No signs of toxic megacolon

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 18 U/L (normal 0 to 35)

[redacted] **20[redacted] BACTERIA (URINE):** 220-750/UL

[redacted] **20[redacted] BACTERIOLOGY AND VIROLOGY (STOOL):** Negative: No organisms identified

[redacted] **20[redacted] COLONOSCOPY:** No normal mucosa (pancolitis)

[redacted] **20[redacted] CREATININE:** 88 MMOL/L (normal 64 to 104)

[redacted] **20[redacted] FECAL CALPROTECTIN (STOOL):** 1633 UG/G (normal 0 to 50)

[redacted] **20[redacted] HEMOGLOBIN:** 8.1 MMOL/L (normal 8.5 to 10)

[redacted] **20[redacted] HEMOGLOBIN:** 8.2 MMOL/L (normal 8.5 to 11.0)

[redacted] **20[redacted] HEMOGLOBIN:** 10.6 MMOL/L (normal 8.5 to 11.0)

[redacted] **20[redacted] POTASSIUM:** 4.1 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] RED BLOOD CELLS (URINE):** Results: 22/UL Lower normal range: 0 Upper normal range: 18

[redacted] **20[redacted] RED BLOOD CELLS (URINE):** 42 /uL (normal 0 to 18)

[redacted] **20[redacted] SODIUM:** 142 MMOL/L (normal 136 to 145)

[redacted] **20[redacted] WHITE BLOOD CELLS (URINE):** Results: >900/UL Lower normal range: 0 Upper normal range: 10

[redacted] **20[redacted] WHITE BLOOD CELLS (URINE):** 32 /uL (normal 0 to 10)

[redacted] **20[redacted] WHITE BLOOD CELLS (URINE):** 17.21 X10**9/L (normal 4.00 to 10.00)

[redacted] **20[redacted] WHITE BLOOD CELLS (URINE):** 76 /uL (normal 0 to 10)

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
潰瘍性大腸炎	X	X		
鉄欠乏性貧血				X

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

Medical History	Onset Year
DIVERTICULITIS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
EYE DISEASE/DISORDER: GLAUCOMA	20[redacted]
HYPERTENSION	20[redacted]
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
OTHER: BURSITIS OLECRANI	20[redacted]
OTHER: GOUT	20[redacted]
OTHER: JAW PROCEDURE	20[redacted]
OTHER: ROOT DISORDER MOUTH	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	45	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 30 mg	30	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 8	8

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE	NOT REPORTED	OTHER: NO DATA AVAILABLE	Y-M: 20[redacted]
MESALAZINE	60 g	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]
CICLOSPORIN	175 mg	BID	Y-M: 20[redacted]
MERCAPTOPURINE	75 mg	QD	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]
SULFAMETHOXAZOLE;TRIMETHOPRIM	960 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
NIFEDIPINE	30 mg	QD	Y-M: 20[redacted]
TIMOLOL;TRAVOPROST	40 OTHER: MCG/ML	BID	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BECLOMETASONE	0.03 mg/kg	QD	Y-M: 20[redacted] / -30
PREDNISONE	40 mg	QD	Y: 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
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 7
NIFEDIPINE	30 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 7
TIMOLOL;TRAVOPROST	40 OTHER: MCG/ML	BID	Y-M: 20[redacted]	ONGOING
BECLOMETASONE	0.03 mg/kg	QD	Y-M: 20[redacted] / -30	Y-M: 20[redacted] / -15
ANTIBIOTICS	UNK mg	OTHER: UNK	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 16
MORPHINE	10 mg	PRN	Y-M: 20[redacted] / 11	ONGOING
PROPOFOL	100 mg	QD	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 11
MAGNESIUM	2000 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 12

OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 35
SODIUM CHLORIDE	3 L	QD	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 24
IOPROMIDE	80 mL	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 14
LIDOCAINE	UNKNOWN mL	PRN	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 65
IPRATROPIUM;SALBUTAMOL	2.5 mL	QID	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 30
OXYCODONE	10 mg	PRN	Y-M: 20[redacted] / 15	ONGOING
IOPROMIDE	80 mL	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 17
RED BLOOD CELLS	2 OTHER: UNITS	OTHER: SINGLE TRANSFUSION	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 17
ONDANSETRON	UNKNOWN mg	OTHER: UNKNOWN	Y-M: 20[redacted] / 18	Y-M: 20[redacted] / 18
FUROSEMIDE	40 mg	QD	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 21
OTHER NUTRIENTS	83 mL	OTHER: PER HOUR	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 24
POTASSIUM	30 mmol	TID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21
POTASSIUM	30 mmol	TID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 22
METOCLOPRAMIDE	10 mg	TID	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 30
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	NOT REPORTED	PRN	Y-M: 20[redacted] / 24	ONGOING
COLESTYRAMINE	4 g	TID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 27
MIDAZOLAM	5 mg	QID	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
ONDANSETRON	8 mg	TID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 31
POTASSIUM	30 mmol	TID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 31
IOPROMIDE	80 mL	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 30
ONDANSETRON	8 mg	TID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 31
LOPERAMIDE	2 mg	QID	Y-M: 20[redacted] / 32	ONGOING
LOPERAMIDE	4 mg	QID	Y-M: 20[redacted] / 33	ONGOING
ACETYLCYSTEINE	600 mg	QD	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 19
NUTRIENTS NOS	1 OTHER: PACKAGE	PRN	Y-M: 20[redacted] / 5	ONGOING
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 5	ONGOING
SODIUM CHLORIDE	3 L	QD	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 6
GLUCOSE;SODIUM CHLORIDE	3 L	QD	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 8
GLUCOSE;SODIUM CHLORIDE	2 L	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 12
IRON	1000 mg	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 9

NADROPARIN	0.3 mL	QD	Y-M: 20[redacted] / 9	ONGOING
POTASSIUM	40 mmol	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 30
BUPRENORPHINE	0.2 mg	OTHER: 6 TIMES DAILY	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 41
IOPROMIDE	100 mL	OTHER: ONE TIME ONLY	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 37
LIDOCAINE	UNKNOWN mg	OTHER: UNKNOWN	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 65
METAMIZOLE	1000 mg	QID	Y-M: 20[redacted] / 41	ONGOING
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 41	ONGOING
LIDOCAINE	10 mL	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 45	ONGOING
MIDAZOLAM	2.5 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 49	ONGOING
GENTAMICIN	320 mg	QD	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
PROPOFOL	100 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 52	ONGOING
CLONIDINE	75 OTHER: MICROGRAM	BID	Y-M: 20[redacted] / 55	ONGOING
VANCOMYCIN	500 mg	QID	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 59
VANCOMYCIN	1000 mg	BID	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 62

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

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 6
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 8): Albumin: 30 [35 - 50] G/L; Calcium: 2.01 [2.2 - 2.6] MMOL/L; Hemoglobin: 103.12576 [136.9639 - 169.1907] G/L; NPTST159-CRP: 39.7 [0 - 5] MG/L; NPTST314-LEUKOCYTES: 11.1 [4 - 10.5] 10E9/L; NPTST319-MAGNESIUM: 0.71 [0.75 - 1.03] MMOL/L; NPTST391-PHOSPHATE: 0.67 [0.81 - 1.45] MMOL/L; NPTST513-UREUM: 1.2 [2.9 - 8.2] MMOL/L; Potassium: 3 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 9): Albumin: 26 [35 - 50] G/L; Calcium: 2 [2.2 - 2.6] MMOL/L; Hemoglobin: 93.45772 [136.9639 - 169.1907] G/L; NPTST159-CRP: 38.1 [0 - 5] MG/L; NPTST297-IRON: 2.6 [11 - 32] UMOL/L; NPTST314-LEUKOCYTES: 9.9 [4 - 10.5] 10E9/L; NPTST319-MAGNESIUM: 0.70 [0.75 - 1.03] MMOL/L; NPTST361-OTYV(IRON SATURATION): 0.10 [0.2 - 0.55] UNIT NOT REPORTED; NPTST391-PHOSPHATE: 0.61 [0.81 - 1.45] MMOL/L; NPTST494-TRANSFERRIN: 1.02 [2 - 3.6] G/L; NPTST507-TYBC (TOTAL IRON BINDING COMPLE: 25.7 [50 - 91] UMOL/L; NPTST513-UREUM: 2.2 [2.9 - 8.2] MMOL/L; Potassium: 3.4 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 10): Albumin: 27 [35 - 50] G/L; Calcium: 1.97 [2.2 - 2.6] MMOL/L; Hemoglobin: 93.45772 [136.9639 - 169.1907] G/L; NPTST159-CRP: 39.1 [0 - 5] MG/L; NPTST314-LEUKOCYTES: 11.0 [4 - 10.5] 10E9/L; NPTST319-MAGNESIUM: 0.66 [0.75 - 1.03] MMOL/L; NPTST391-PHOSPHATE: 0.86 [0.81 - 1.45] MMOL/L; NPTST513-UREUM: 1.9 [2.9 - 8.2] MMOL/L; Potassium: 3.4 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 11): NPTST397-PO2 VENOUS: 3.2 [10 - 13.3] KPA; [redacted]20[redacted] (RX DAY 12): Hemoglobin: 91.84638 [136.9639 - 169.1907] G/L; NPTST319-MAGNESIUM: 0.63 [0.75 - 1.03] MMOL/L; Potassium: 4

[3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 13): NPTST319-MAGNESIUM: 0.94 [0.75 - 1.03] MMOL/L; [redacted]20[redacted] (RX DAY 14): Creatinine: 66 [75 - 110] UMOL/L; Hemoglobin: 93.45772 [136.9639 - 169.1907] G/L; NPTST159-CRP: 288.7 [0 - 5] MG/L; NPTST314-LEUKOCYTES: 27.8 [4 - 10.5] 10E9/L; Potassium: 5.5 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 17): Hemoglobin: 77.34432 [136.9639 - 169.1907] G/L; NPTST159-CRP: 101 [0 - 5] MG/L; NPTST314-LEUKOCYTES: 24.3 [4 - 10.5] 10E9/L; [redacted]20[redacted] (RX DAY 18): Hemoglobin: 95.06906 [136.9639 - 169.1907] G/L; [redacted]20[redacted] (RX DAY 21): Creatinine: 48 [75 - 110] UMOL/L; Hemoglobin: 104.7371 [136.9639 - 169.1907] G/L; NPTST159-CRP: 49.4 [0 - 5] MG/L; NPTST314-LEUKOCYTES: 24.0 [4 - 10.5] 10E9/L; NPTST319-MAGNESIUM: 0.78 [0.75 - 1.03] MMOL/L; NPTST391-PHOSPHATE: 0.67 [0.81 - 1.45] MMOL/L; Potassium: 2.7 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 22): Hemoglobin: 103.12576 [136.9639 - 169.1907] G/L; NPTST159-CRP: 27 [0 - 5] MG/L; NPTST314-LEUKOCYTES: 24.1 [4 - 10.5] 10E9/L; Potassium: 4.3 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 23): Potassium: 3.9 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 27): Creatinine: 54 [75 - 110] UMOL/L; Hemoglobin: 87.01236 [136.9639 - 169.1907] G/L; [redacted]20[redacted] (RX DAY 29): Albumin: 33 [35 - 50] G/L; Calcium: 2.18 [2.2 - 2.6] MMOL/L; Creatinine: 54 [75 - 110] UMOL/L; Hemoglobin: 93.45772 [136.9639 - 169.1907] G/L; NPTST319-MAGNESIUM: 0.64 [0.75 - 1.03] MMOL/L; NPTST391-PHOSPHATE: 0.84 [0.81 - 1.45] MMOL/L; Potassium: 2.8 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 30): NPTST159-CRP: 91.7 [0 - 5] MG/L; NPTST319-MAGNESIUM: 0.65 [0.75 - 1.03] MMOL/L; Potassium: 3.7 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 31): NPTST319-MAGNESIUM: 0.62 [0.75 - 1.03] MMOL/L; [redacted]20[redacted] (RX DAY 32): Creatinine: 56 [75 - 110] UMOL/L; NPTST319-MAGNESIUM: 0.62 [0.75 - 1.03] MMOL/L; [redacted]20[redacted] (RX DAY 34): Albumin: 28 [35 - 50] G/L; Calcium: 2.13 [2.2 - 2.6] MMOL/L; Creatinine: 51 [75 - 110] UMOL/L; [redacted]20[redacted] (RX DAY 38): Creatinine: 51 [75 - 110] UMOL/L; NPTST159-CRP: 101.1 [0 - 5] MG/L; NPTST314-LEUKOCYTES: 25.6 [4 - 10.5] 10^9/L; Potassium: 4.9 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 41): Creatinine: 49 [75 - 110] UMOL/L; Hemoglobin: 87.01236 [136.9639 - 169.1907] G/L; NPTST159-CRP: 89.2 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 45): Creatinine: 52 [75 - 110] UMOL/L; Hemoglobin: 82.17834 [136.9639 - 169.1907] G/L; NPTST159-CRP: 52.2 [0 - 5] MG/L; NPTST314-LEUKOCYTES: 16.1 [4 - 10.5] 10^9/L; Potassium: 4.8 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 51): Albumin: 29 [35 - 50] G/L; Creatinine: 53 [75 - 110] UMOL/L; NPTST159-CRP: 101.8 [0 - 5] MG/L; NPTST314-LEUKOCYTES: 19.2 [4 - 10.5] 10^9/L; Potassium: 5.3 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 53): NPTST391-PHOSPHATE: 1.67 [0.81 - 1.45] MMOL/L; Potassium: 4.6 [3.5 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 59): Creatinine: 51 [75 - 110] UMOL/L; [redacted]20[redacted] (RX DAY 62): Albumin: 30 [35 - 50] G/L; NPTST319-MAGNESIUM: 0.56 [0.75 - 1.03] MMOL/L; [redacted]20[redacted] (RX DAY 63): NPTST314-LEUKOCYTES: 11.6 [4 - 10.5] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 11): SUBTOTAL COLECTOMY WITH ILEOSTOMY: COMPLICATIONS AFTER SURGERY: FEVER, DYSPNEA AND ELEVATED CRP. ADDITIONAL COMPLICATIONS: NECROTIC OMENTUM AND ABDOMINAL ABCESS. SURGICAL DRAINAGE OF ABCESS AND REMOVAL OF NECTROTIC OMENTUM WAS DONE ON [redacted] [redacted] 20[redacted]. PATIENT RECOVERED AND WAS DISCHARGED ON [redacted] [redacted] 20[redacted].; [redacted]20[redacted] (RX DAY 14): CT ABDOMEN: EXTENSIVE INTRA-ABDOMINAL INFECTED FLUID COLLECTIONS POST SURGERY; [redacted]20[redacted] (RX DAY 17): CT ABDOMEN: PARA COLIC COLLECTION RIGHT SIDE ADEQUATELY DRAINED. SUPRA FECICAL COLLECTION HAS A RESIDUAL REMAINDER (7X3 CM); [redacted]20[redacted] (RX DAY 22): CT ABDOMEN: NO FLUID COLLECTIONS TO BE DRAINED; [redacted]20[redacted] (RX DAY 30): CT ABDOMEN: NO NEW FLUID COLLECTIONS. EXTENDED STOMACH WITHOUT CLEAR OBSTRUCTION.; [redacted]20[redacted] (RX DAY 36): CT ABDOMEN: FLUID COLLECTION IN RIGHT ABDOMEN SLIGHTLY MORE VOLUME, INCREASED AIR AND DEBRIS. NO NEW FLUID COLLECTIONS.

AE Stopped Rx Day	154 (146 DAYS AFTER LAST TREATMENT)
Duration of AE	149 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	DISEASE UNDER STUDY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #2: Event of Interest - Anemia

Event Description	IRON DEFICIENCY ANEMIA
Preferred term	鉄欠乏性貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 8
Age at AE Onset	6[redacted]
Laboratory Testing	

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はオランダの 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，憩室炎及び潰瘍性大腸炎であった。

Event 1 の臨床経過：

投与6日後＊　　，被験者は潰瘍性大腸炎の悪化を発現した。投与154日後＊　　，潰瘍性大腸炎の悪化は消失した。

投与6日後＊　　，被験者は脱水，発熱，電解質失調，貧血及び低アルブミン血症があり，入院した。徴候及び症状には，体重減少及び嘔吐も含まれた。投与11日後＊　　，被験者は回腸瘻造設及びハルトマン手術を伴う結腸亜全摘術を受けた。術後の合併症は，発熱，呼吸困難及びCRP 上昇であった。更なる合併症としては，大網壊死及び腹部膿瘍が含まれた。　　投与52日後＊，被験者は壊死した大網の除去及び膿瘍のドレナージを受けた。投与65日後＊　　，被験者は退院した。

投与された薬剤及び処置は，生理食塩液（塩化ナトリウム 0.9%），生理食塩液（塩化ナトリウム 0.45%）＋ブドウ糖（2.5%），フェインジェクト，塩化カリウム，マグネシウム，赤血球濃厚液，オンダンセトロン，経腸経管栄養，メトクロプラミド，コレスチラミン，フラジール，ceftriaxon，モルヒネ，オキノーム，オキシコンチン，ロペラミド，ゲンタマイシン，クロニジン，バンコマイシン，アセチルシステイン及びサルブタモール・イプラトロピウム合剤であった。

The patient's past medications include:

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

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

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

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

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

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

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

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

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

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

Causality for ABT-494 (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: Disease under study.

- AbbVie: Recurring flare of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 30 G/L (normal 35 to 50)

[redacted] **20[redacted] ALBUMIN:** 26 G/L (normal 35 to 50)

[redacted] **20[redacted] ALBUMIN:** 29 G/L (normal 35 to 50)

[redacted] **20[redacted] CALCIUM:** 2.01 MMOL/L (normal 2.2 to 2.6)

[redacted] **20[redacted] CALCIUM:** 1.97 MMOL/L (normal 2.2 to 2.6)

[redacted] **20[redacted] CRP:** 39.7 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 39.1 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 52.2 MG/L (normal 0 to 5)

[redacted] **20[redacted] CT ABDOMEN:** extensive intra-abdominal infected fluid collections post surgery

[redacted] **20[redacted] CT ABDOMEN:** para colic collection right side adequately drained. Supra fecical collection has a residual remainder (7x3cm)

[redacted] **20[redacted] CT ABDOMEN:** no fluid collections to be drained

[redacted] **20[redacted] CT ABDOMEN:** no new fluid collections. extended stomach without clear obstruction

[redacted] **20[redacted] CT ABDOMEN:** fluid collection in right abdomen slightly more volume, increased air and debris. No new fluid collections.

[redacted] **20[redacted] HEMOGLOBIN:** 6.4 MMOL/L (normal 8.5 to 10.5)

[redacted] **20[redacted] HEMOGLOBIN:** 5.8 MMOL/L

[redacted] **20[redacted] HEMOGLOBIN:** 5.4 MMOL/L

[redacted] **20[redacted] HEMOGLOBIN:** 5.1 MMOL/L

[redacted] **20[redacted] IRON:** 2.6 MCMOL/L (normal 11 to 32)

[redacted] **20[redacted] LEUKOCYTES:** 11.1 X10**9/L (normal 4 to 10.5)

[redacted] **20[redacted] LEUKOCYTES:** 24.1 X10**9/L (normal 4 to 10.5)

[redacted] **20[redacted] LEUKOCYTES:** 25.6 X10**9/L (normal 4 to 10.5)

[redacted] **20[redacted] MAGNESIUM:** 0.71 MMOL/L (normal 0.75 to 1.03)

[redacted] **20[redacted] MAGNESIUM:** 0.66 MMOL/L (normal 0.75 to 1.03)

[redacted] **20[redacted] MAGNESIUM:** 0.56 MMOL/L (normal 0.75 to 1.03)

[redacted] **20[redacted] PHOSPHATE:** 0.67 MMOL/L (normal 0.81 to 1.45)

[redacted] **20[redacted] POTASSIUM:** 3.0 MMOL/L (normal 3.5 to 4.5)

[redacted] **20[redacted] POTASSIUM:** 3.4 MMOL/L (normal 3.5 to 4.5)

[redacted] **20[redacted] POTASSIUM:** 4.9 MMOL/L (normal 3.5 to 4.5)

[redacted] **20[redacted] TOTAL IRON BINDING COMPLEX:** 25.7 MCMOL/L (normal 50 to 91)

[redacted] **20[redacted] UREUM:** 1.2 MMOL/L (normal 2.9 to 8.2)

[redacted] **20[redacted] UREUM:** 1.9 MMOL/L (normal 2.9 to 8.2)

[redacted] **20[redacted] VENOS PO2:** 3.2 KPA (normal 10 to 13.3)

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
尿路性敗血症	X			X

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

Medical History	Onset Year
BENIGN PROSTATIC HYPERPLASIA	20[redacted]
DEPRESSION: MIDDLE GRAD	19[redacted]
DIABETES MELLITUS: TYP 2	20[redacted]
EYE DISEASE/DISORDER: CATARACTAPOSTERIOR BOTH EYES , OPERATION [redacted] /20[redacted]	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: GRADE 2	19[redacted]
HYPERLIPIDEMIA	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: CRONICAL CERVICOTHORACAL PAIN SYNDROM	19[redacted]
OTHER: MICRO HAEMATURIE	20[redacted]
OTHER: MICRO HEMATURIA	20[redacted]
OTHER: OVERWEIGHT	20[redacted]
OTHER: VITAMIN B12 DEFICIENCY	20[redacted]
SLEEP APNEA: CPAP NEEDED	20[redacted]
TUBERCULOSIS: LATENT [redacted]/20[redacted] QUANTIFERON TEST POSITIV, NO SIGNS IN X RAY ,TREATED WITH ISONIAZID [redacted]/20[redacted]-[redacted]/20[redacted]	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	40	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 15 mg	15	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
BUDESONIDE	2 g	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]
MESALAZINE	2000 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted]
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
LISINOPRIL	2.5 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
CICLOSPORIN	200 mg	QD	Y-M: 20[redacted]
CICLOSPORIN	400 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
PREDNISONE	50 mg	QD	Y-M: 20[redacted]
SULFAMETHOXAZOLE;TRIMETHOPRIM	800 mg	OTHER: 3 TIMES A WEEK	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
MESALAZINE	4500 mg	TID	Y-M: 20[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -77
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -80
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 OTHER: UNITS	BID	Y-M: 20[redacted] / -10
PROPOFOL	360 mg	QD	Y-M: 20[redacted] / -9

ESOMEPRAZOLE	20 mg	QD	Y: 19[redacted]
PARACETAMOL	2000 mg	PRN	Y: 19[redacted]
MIANSERIN	30 mg	QD	Y: 19[redacted]
SERTRALINE	175 mg	TID	Y: 19[redacted]
INSULIN LISPRO	AS NEEDED IU	OTHER: PER PLAN	Y: 20[redacted]
LOPERAMIDE	2 mg	PRN	Y: 20[redacted]
ALFUZOSIN	10 mg	QD	Y: 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	100 mg	QD	Y-M: 20[redacted]	ONGOING
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted]	ONGOING
LISINOPRIL	2.5 mg	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	4500 mg	TID	Y-M: 20[redacted]	ONGOING
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -77	Y-M: 20[redacted] / 43
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -80	Y-M: 20[redacted] / 43
PREDNISONE	25 mg	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 56
LEVOFLOXACIN	1000 mg	BID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 62
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 57	ONGOING
ESOMEPRAZOLE	20 mg	QD	Y: 19[redacted]	ONGOING
PARACETAMOL	2000 mg	PRN	Y: 19[redacted]	ONGOING
MIANSERIN	30 mg	QD	Y: 19[redacted]	ONGOING
SERTRALINE	175 mg	TID	Y: 19[redacted]	ONGOING
INSULIN LISPRO	AS NEEDED IU	OTHER: PER PLAN	Y: 20[redacted]	ONGOING
LOPERAMIDE	2 mg	PRN	Y: 20[redacted]	ONGOING
ALFUZOSIN	10 mg	QD	Y: 20[redacted]	ONGOING

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

Event Description	SEPTIC URINARY TRACT INFECTION
Preferred term	尿路性敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 53
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 53): ABDOMINAL ULTRASOUND: PROSTATAHYPERPLASY ,; CT SCAN: PROSTATAHYPERPLASY; ECG: SINUS RHYSM; [redacted]20[redacted] (RX DAY 56): ABDOMINAL ULTRASOUND: BLOCADE OF URIN

AE Stopped Rx Day	62
Duration of AE	10 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はスイスの 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，敗血症性尿路感染の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 40 年間），2 型糖尿病，潰瘍性大腸炎，良性前立腺肥大症，顕微鏡的血尿及び過体重であった。

Event 1 の臨床経過：

投与53日後＊　，被験者は敗血症性尿路感染を発現した。投与62日後＊　，敗血症性尿路感染は消失した。

投与53日後＊　，被験者は失神，疼痛，尿閉及び尿路性敗血症の徴候及び症状があり，入院した。尿道カテーテルを挿入し，抗感染症薬の服用を開始した。投与62日後＊　，被験者は退院した。

投与された薬剤は tavanic であった。

The patient's past medications include:

BUDENOFALK FOAM for ULCERATIVE COLITIS ([redacted])

SALOFALK FOAM for ULCERATIVE COLITIS ([redacted])

SALOFALK SUPP for ULCERATIVE COLITIS ([redacted])

ISONIAZID for LATENT TUBERCULOSIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

SANDIMMUN for ULCERATIVE COLITIS ([redacted])

SOLU MEDROL for ULCERATIVE COLITIS ([redacted])

PREDNISON for ULCERATIVE COLITIS ([redacted])

BACTRIM for PROPHYLAXIS ([redacted])

CORTIMENT for ULCERATIVE COLITIS ([redacted])

PREDNISON for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Blinded)

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1) Urosepsis (10048709) (Urosepsis (10048709)) [v.22.1] [10048709]

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 ABT-494 (Blinded)

Event of SEPTIC URINARY TRACT INFECTION

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** PROSTATIC HYPERPLASIA

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Blockade of urine

[redacted] **20[redacted] CT SCAN:** PROSTATIC HYPERPLASIA

[redacted] **20[redacted] ECG:** SinuRhythm

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
潰瘍性大腸炎	X	X		
サイトメガロウイルス感染				X

Treatment Group	Age at Study Start	Sex	Race
Placebo	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
EYE DISEASE/DISORDER: KONJUNKTIVITIS	20[redacted]
OTHER: HERPES LABIALIS	20[redacted]
OTHER: MOLLUSCUM CANTAGIOSUM AT ABDOMEN, FACE AND BACK	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 17	17

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
MESALAZINE	3 g	QD	Y-M: 20[redacted]
PREDNISONE	50 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BUDESONIDE	2 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
CALCIUM	1000 mg	QD	Y-M: 20[redacted] / -293
GOLIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -293
MERCAPTOPURINE	50 mg	QD	Y-M: 20[redacted] / -293
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -300
SULFAMETHOXAZOLE;TRIMETHOPRIM	800 mg	OTHER: 3 TIMES / WEEK	Y-M: 20[redacted] / -154
BUDESONIDE;SODIUM CHLORIDE	2.3 mg	QD	Y-M: 20[redacted] / -158
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -158
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / -160
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -160
CEFTRIAXONE	2000 mg	QD	Y-M: 20[redacted] / -161
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -161
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -161
BUDESONIDE	2 mg	QD	Y-M: 20[redacted] / -112
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	BID	Y-M: 20[redacted] / -8
INTRAUTERINE CONTRACEPTIVE DEVICE	1 OTHER: SPIRAL	PRN	Y: 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
MESALAZINE	3 g	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 15
CALCIUM	1000 mg	QD	Y-M: 20[redacted] / -293	Y-M: 20[redacted] / 14
MERCAPTOPURINE	50 mg	QD	Y-M: 20[redacted] / -293	Y-M: 20[redacted] / -15
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	BID	Y-M: 20[redacted] / -8	Y-M: 20[redacted] / -8
CALCIUM CARBONATE;COLECALCIFEROL	500 mg	QD	Y-M: 20[redacted] / 15	ONGOING

ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 25
METHYLPREDNISOLONE	50 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 26
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
SODIUM CHLORIDE	500 mL	OTHER: 24 H	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 22
ASCORBIC ACID;BIOTIN;CALCIUM;COPPER;CYANOCOBALAMIN;ERGOCALCIFEROL;FOLIC ACID;IRON;MAGNESIUM;MANGANESE;MOLYBDENUM;NICOTINAMIDE;PANTOTHENIC ACID;PHOSPHORUS;PYRIDOXINE;RETINOL;RIBOFLAVIN;THIAMINE;TOCOPH	1 OTHER: TABLET	BID	Y-M: 20[redacted] / 16	ONGOING
BUDESONIDE	2 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 32
CARBOHYDRATES NOS;FATTY ACIDS NOS;MINERALS NOS;PROTEINS NOS;VITAMINS NOS	500 mL	OTHER: 24 H	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 18
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 19
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 16
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 19
OXYCODONE	3 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 16
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / 16	ONGOING
PARACETAMOL	500 mg	QID	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 17
THIAMINE	300 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 22
METAMIZOLE	1000 mg	QD	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 17
PHOSPHORIC ACID	10 mL	BID	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 18
PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / 18	Y-M: 20[redacted] / 18
CARBOHYDRATES NOS;CHOLINE;FATS NOS;MINERALS NOS;PROTEINS NOS;VITAMINS NOS	500 mL	OTHER: 24 H	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
INSULIN ASPART	2 IU	QD	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
PHOSPHORIC ACID	10 mL	QID	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 21
SIMETICONE	42 mg	TID	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
AMOXICILLIN	1000 mg	BID	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 29
CARBOHYDRATES NOS;FATTY ACIDS NOS;MINERALS NOS;PROTEINS NOS;VITAMINS NOS	200 mL	BID	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 20
CLARITHROMYCIN	500 mg	BID	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 29
NUTRIENTS NOS	1 OTHER: DRINK	OTHER: AS NEEDED	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 23
INSULIN ASPART	2 IU	QD	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21

PHOSPHORIC ACID	10 mL	QD	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 22
INSULIN ASPART	2 IU	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
THIAMINE	100 mg	QD	Y-M: 20[redacted] / 23	ONGOING
INSULIN ASPART	4 IU	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 24
IRON	100 mg	QD	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 25
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 33
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	1000 mL	OTHER: 24 H	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 41
CLEMASTINE	2 mg	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 33
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 33	ONGOING
INFLIXIMAB	300 mg	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 33
INSULIN ASPART	2 IU	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 34
IRON	500 mg	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 33
METHYLPREDNISOLONE	125 mg	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 33
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 33
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 42
PARACETAMOL	1000 mg	QID	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 42
INSULIN ASPART	4 IU	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 35
INSULIN ASPART	2 IU	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 39
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 36
COLECALCIFEROL	8 gtt	QD	Y-M: 20[redacted] / 37	ONGOING
METAMIZOLE	500 mg	BID	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 37
BUDESONIDE	2 mg	BID	Y-M: 20[redacted] / 38	ONGOING
INFLIXIMAB	200 mg	QD	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 38
MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 43
GANCICLOVIR	250 mg	BID	Y-M: 20[redacted] / 40	ONGOING
INSULIN ASPART	2 IU	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 40
INSULIN ASPART	3 IU	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 40
METAMIZOLE	500 mg	BID	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 40
INSULIN ASPART	4 IU	QD	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 41
INSULIN ASPART	2 IU	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 43
INSULIN ASPART	3 IU	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
METHYLPREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 46
INSULIN ASPART	3 IU	QD	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 45
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 46
INSULIN ASPART	2 IU	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 46

INSULIN ASPART	5 IU	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 46
METAMIZOLE	500 mg	BID	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 46
PLANTAGO OVATA	1 OTHER: SACHET	QD	Y-M: 20[redacted] / 46	ONGOING
METHYLPREDNISOLONE	25 mg	QD	Y-M: 20[redacted] / 47	ONGOING
INTRAUTERINE CONTRACEPTIVE DEVICE	1 OTHER: SPIRAL	PRN	Y: 20[redacted]	ONGOING

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

Event Description	WORSENING COLITIS ULCEROSA
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 15
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 15): Albumin: 24 [35 - 52] G/L; Leukocytes: 10.9 [3 - 10.5] 10^9/L; NPTST159-CRP: 59 [0 - 5] MG/L; NPTST297-IRON: 4.7 [6.6 - 26] UMOL/L; Platelets: 302 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 16): Erythrocytes: 3.83 [3.9 - 5] 10^12/L; Glucose: 6.1 [4.11 - 5.89] MMOL/L; Glucose: 8.9 [4.11 - 5.89] MMOL/L; Hemoglobin: 113 [121 - 154] G/L; [redacted]20[redacted] (RX DAY 17): Glucose: 6.3 [4.11 - 5.89] MMOL/L; Glucose: 9.4 [4.11 - 5.89] MMOL/L; NPTST295-INORGANIC PHOSPHAT: 0.70 [0.81 - 1.45] MMOL/L; [redacted]20[redacted] (RX DAY 18): Glucose: 6.7 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 19): Glucose: 15 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 20): Glucose: 6 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 21): Glucose: 13.5 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 22): Glucose: 6.3 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 23): Glucose: 14.5 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 24): Glucose: 15.5 [4.11 - 5.89] MMOL/L; Glucose: 5.9 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 25): Glucose: 6.7 [4.11 - 5.89] MMOL/L; Glucose: 12.8 [4.11 - 5.89] MMOL/L

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[redacted]20[redacted] (RX DAY 15): OTHER BIOPSY NPTST254-HELIOBACTER POSITIV: POSITIVE-HELIOBACTER POSITIV

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[redacted]20[redacted] (RX DAY 15): COLONOSCOPY: TOTAL MAYO SCORE IS SEVERE, 40 CM AB ANO; GASTROSCOPY: MILD GASTRITIS WITH HELIOBACTER POSITIV; X-RAY ABDOMEN: STOOL AND GAS IN COLON; [redacted]20[redacted] (RX DAY 16): X-RAY ABDOMEN: STOOL AND GAS IN COLON; [redacted]20[redacted] (RX DAY 17): X-RAY ABDOMEN: STOOL AND GAS IN COLON

AE Stopped Rx Day	26 (9 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DETAILS SEE IN THE SAE SUPPLEMENTAL FORMS AND AE`S AN CONCOMITTANT MEDICATIONS.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	WORSENING COLITITS ULCEROSA
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 33 (16 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY -14): Alanine Aminotransferase: 16 [9 - 34] U/L; [redacted]20[redacted] (RX DAY 1): Alanine Aminotransferase: 21 [9 - 34] U/L; [redacted]20[redacted] (RX DAY 33): Aspartate Aminotransferase: 49 [0 - 35] U/L; Glucose: 10.8 [4.11 - 5.89] MMOL/L; NPTST159-CRP: 35 [0 - 5] MG/L; Platelets: 223 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 34): Erythrocytes: 3.83 [3.9 - 5] 10^12/L; Glucose: 5.9 [4.11 - 5.89] MMOL/L; Glucose: 11.2 [4.11 - 5.89] MMOL/L; Hemoglobin: 114 [121 - 154] G/L; [redacted]20[redacted] (RX DAY 35): Glucose: 13.4 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 36): Glucose: 11 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 37): Glucose: 9.7 [4.11 - 5.89] MMOL/L; Glucose: 8.4 [4.11 - 5.89] MMOL/L; NPTST494-TRANSFERRIN: 2.0 [1.78 - 3.6] G/L; [redacted]20[redacted] (RX DAY 38): Glucose: 8.2 [4.11 - 5.89] MMOL/L; Glucose: 9.5 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 39): Glucose: 8.3 [4.11 - 5.89] MMOL/L; Glucose: 11.9 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 40): Glucose: 10 [4.11 - 5.89] MMOL/L; Glucose: 9.1 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 41): Glucose: 14.2 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 42): Glucose: 10.7 [4.11 - 5.89] MMOL/L; Glucose: 12 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 43): Glucose: 11.7 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 45): Glucose: 9.4 [4.11 - 5.89] MMOL/L; [redacted]20[redacted] (RX DAY 46): Glucose: 12.5 [4.11 - 5.89] MMOL/L; Glucose: 11.2 [4.11 - 5.89] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 40): OTHER BIOPSY NPTST171-CYTOMEGALO VIRUS: POSITIVE-CYTOMEGALO VIRUS INFECTION

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 33): X-RAY ABDOMEN: GRADUALLY DILATED AND CHAIR-FILLED COECUM AND ASCENDING COLON, AS A RESULT OF THE INFLOW OF THE METEORIC SMALL INTESTINE. NO FREE STANDING AIR.; [redacted]20[redacted] (RX DAY 34): X-RAY ABDOMEN: PRONOUNCED COPROSTASIS. NO ILEUS SIGNS. NO FREE INTRA-ABDOMINAL AIR.; [redacted]20[redacted] (RX DAY 36): X-RAY ABDOMEN: NORMAL; [redacted]20[redacted] (RX DAY 37): COLONOSCOPY: ENDOSCOPY SCORE 3. SEVERE FROM RECTUM TO 40 CM AB ANO IN THE SIGMOID. A LITTLE BIT BETTER TO THE COLONOSCOPY ON THE [redacted].[redacted].; [redacted]20[redacted] (RX DAY 40): BIOPSY (LOCATION: RECTUM): CYTOMEGALO VIRUS INFECTION; RECTOSCOPY: ITS A LITTLE BIT BETTER FROM THE COLONOSCOPY ON THE [redacted].[redacted]. ENDOSCOPY SCORE 3. SEVERE. BUT ONLY 15 CM FROM RECTUM TO SIGMOID.

AE Stopped Rx Day	52 (35 DAYS AFTER LAST TREATMENT)
Duration of AE	20 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	WORSENING OF COLITIS ULCEROSA AGAIN. EVERY 2 TIMES TO GO ON TOILET FOR STOOL, DIARRHOE, BLOOD,PAIN ABDOMEN, CRP INCREASED. NO FEVER.HOSPITALISATION AGAIN. PANCOLITIS WITH CYTOMEGALOVIRUS INFECTION.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Event of Interest - Opportunistic infections	
Event Description	CYTOMEGALO VIRUS INFECTION
Preferred term	サイトメガロウイルス感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 40 (23 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:25
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はスイスの 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側）であった。

Event 1 の臨床経過：

投与8日後＊　　，被験者は潰瘍性大腸炎の悪化（非重篤）を発現し，投与14日後＊　　に消失した。

投与15日後＊　　，被験者は潰瘍性大腸炎の悪化を発現した。投与26日後＊　　，潰瘍性大腸炎の悪化は消失した。

投与15日後＊　　，潰瘍性大腸炎の悪化，血性下痢及び疲労のため，入院した。徴候及び症状は，栄養障害，腹痛，低リン酸血症，高血糖，血清鉄の低値及びヘリコバクター・ピロリ菌抗体検査陽性の軽度の胃炎であった。投与15日後＊　　，被験者は結腸内視鏡検査，内視鏡検査，臨床検査及び腹部 X 線検査を受けた。投与26日後＊，被験者は退院した。

投与された薬剤は，アモキシシリン，benerva，クレキサン，fresubin，isostar，klacid，メトロニダゾール，塩化ナトリウム，perfalgan，phosphat，ロセフィン，ソル・メドロール，survimed，budenofalk，ノボラピッド，オキノーム，flatulex，novalgin，プリンペラン，venofer 及び prednison であった。

The patient's past medications include:

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

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

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

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

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

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

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

PURI NETHOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SOLU MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of WORSENING COLITIS ULCEROSA

- Investigator: Data will complete in the next days, so I have more information.

- AbbVie: Recurring flare of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL X-RAY:** STOOL AND GAS IN COLON

[redacted] **20[redacted] ABDOMINAL X-RAY:** STOOL AND GAS IN COLON

[redacted] **20[redacted] ABDOMINAL X-RAY:** STOOL AND GAS IN COLON

[redacted] **20[redacted] ALBUMIN:** 24 G/L (normal 35 to 52)

[redacted] **20[redacted] BIOPSY:** Helicobacter positive

[redacted] **20[redacted] CHEST X-RAY:** Finding(s) Normal; Calcified granulomas - Absent; Pleural scarring- Absent; Pleural thickening - Absent; No Signs of active TB; No finding indicative of previous TB infection.

[redacted] **20[redacted] COLONOSCOPY:** Yes there was a clear demarcation between normal and inflamed colonic mucosa seen; disttance of demarcation from the anal verge 40.

[redacted] **20[redacted] COLONOSCOPY:** TOTAL MAYO SCORE IS SEVERE, 40 CM AB ANO

[redacted] **20[redacted] CRP:** 59 MG/L (normal 0 to 5)

[redacted] **20[redacted] ENDOSCOPY:** MILD GASTRITIS WITH HELIOBACTER POSITIVE

[redacted] **20[redacted] GLUCOSE:** 6.1 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 8.9 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 6.3 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 9.4 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 6.7 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 15.0 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 6.0 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 13.5 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 6.3 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 14.5 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 5.9 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 15.5 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 6.7 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] GLUCOSE:** 12.8 MMOL/L (normal 4.11 to 5.89)

[redacted] **20[redacted] HEMOGLOBIN:** 113 G/L (normal 121 to 154)

[redacted] **20[redacted] INORGANIC PHOSPHATE:** 0.70 MMOL/L (normal 0.81 to 1.45)

[redacted] **20[redacted] IRON:** 4.7 MCMOL/L (normal 6.6 to 26)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.83 T/L (normal 3.9 to 5.0)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 10.0 G/L (normal 3 to 10.5)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はスイスの 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎であった。

Event 2 の臨床経過：

投与8日後＊　　，被験者は潰瘍性大腸炎の悪化（非重篤）を発現し，投与14日後＊　　に消失した。

投与15日後＊　，被験者は潰瘍性大腸炎の悪化を発現し，投与26日後＊　に消失した。

投与33日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与52日後＊　，潰瘍性大腸炎の悪化は消失した。

投与33日後＊　，被験者は潰瘍性大腸炎の悪化があり，再び来院した。被験者は，今回は排便の際に 2 回に 1 回は下痢，血便及び腹痛を伴うと訴え，CRP が上昇していた。発熱は見られなかった。徴候及び症状は，栄養障害，腹痛，高血糖，血清鉄の低値及びヘリコバクター・ピロリ菌抗体検査が陽性の軽度の胃炎であった。被験者は，腹部 X 線検査，結腸内視鏡検査及び直腸鏡検査を受けた。投与52日後＊　，被験者は退院した。

投与された薬剤は，ソル・メドロール，budenofalk rectal foam，レミケード，vi-de 3，transipeg forte，クレキサン及び prednison であった。

The patient's past medications include:

CIPROXIN for ULCERATIVE COLITIS ([redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted])

IMUREK for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

BUDENOFALK RECTAL FOAM for ULCERATIVE COLITIS ([redacted])

GOLIMUMAB for ULCERATIVE COLITIS ([redacted])

PURI NETHOL for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

SPIRICORT for ULCERATIVE COLITIS ([redacted])

BACTRIM FORTE for ULCERATIVE COLITIS ([redacted])

SOLUMEDROL for WORSENING ULCERATIVE COLITIS ([redacted])

METRONIDAZOLE for WORSENING ULCERATIVE COLITIS ([redacted])

ROCEPHIN for WORSENING ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.0] [10009901]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of WORSENING COLITITS ULCEROSA

- Investigator: WORSENING OF COLITIS ULCEROSA AGAIN. EVERY 2 TIMES TO GO ON TOILET FOR STOOL, DIARRHOE, BLOOD,PAIN ABDOMEN, CRP INCREASED. NO FEVER.HOSPITALISATION AGAIN. PANCOLITIS WITH CYTOMEGALOVIRUS INFECTION.

- AbbVie: Recurring flare of pre-existing Ulcerative Colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 49 U/L (normal 0 to 35)

[redacted] **20[redacted] BIOPSY:** cytomegalovirus infection-Positive

[redacted] **20[redacted] COLONOSCOPY:** Endoscopy score 3. severe from rectum to 40 cm ab ano in the sigmoid. a little bit better to the colonoscopy on the [redacted].

[redacted] **20[redacted] CRP:** 35 MG/L (normal 0 to 5.0)

[redacted] **20[redacted] HEMOGLOBIN:** 114 G/L (normal 121 to 154)

[redacted] **20[redacted] PLATELET COUNT:** 223 G/L (normal 150 to 450)

[redacted] **20[redacted] RBC:** 3.83 TI/L (normal 3.9 to 5.0)

[redacted] **20[redacted] RECTOSCOPY**: Its a little bit better from the colonoscopy on the [redacted]. endoscopy score 3. severe. but only 15 cm from rectum to sigmoid.

[redacted] **20[redacted] TRANSFERRIN:** 2.0 G/L (normal 1.78 to 3.6)

[redacted] **20[redacted] X-RAY ABDOMEN:** Gradually dilated and chair-filled coecum and ascending colon, as a result of the inflow of the meteoric small intestine. no free standing air.

[redacted] **20[redacted] X-RAY ABDOMEN:** Pronounced coprostasis. No ileus signs. No free intra-abdominal air.

[redacted] **20[redacted] X-RAY ABDOMEN:** Normal.

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Cytomegalovirus infection: Study drug interrupted.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		
深部静脈血栓症	X			X
肺塞栓症	X			X
ウイルス性咽頭炎	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 45 mg	6[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
KIDNEY DISORDER	20[redacted]
OSTEOPOROSIS	20[redacted]
OTHER: HIGH SUSPICION OF PRIMARY SCEROSING CHOLANGITIS	20[redacted]
OTHER: SUPRARENAL GLAND INSUFFICIENCY	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	15	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 45	45

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	50 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
CALCIUM CARBONATE;COLECALCIFEROL	500/800 OTHER: 500 MG	BID	Y-M: 20[redacted]
TACROLIMUS	6 mg	QD	Y-M: 20[redacted]
IRON	1000 mg	OTHER: ON DEMAND	Y-M: 20[redacted]
HYDROCORTISONE	15 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	3 g	QD	Y-M: 20[redacted]
COLECALCIFEROL	3 (4500 IE/ML) gtt	QD	Y-M: 20[redacted]
ZOLEDRONIC ACID	5MG / 100ML mg	OTHER: YEARLY	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CALCIUM CARBONATE;COLECALCIFEROL	500/800 OTHER: 500 MG	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 71
IRON	1000 mg	OTHER: ON DEMAND	Y-M: 20[redacted]	ONGOING
HYDROCORTISONE	15 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 50
MESALAZINE	3 g	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 97
COLECALCIFEROL	3 (4500 IE/ML) gtt	QD	Y-M: 20[redacted]	ONGOING

ZOLEDRONIC ACID	5MG / 100ML mg	OTHER: YEARLY	Y-M: 20[redacted]	ONGOING
CYAMOPSIS TETRAGONOLOBA	1 OTHER: TEASPOON	QID	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
HYDROCORTISONE	20 mg	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 50
URSODEOXYCHOLIC ACID	450 mg	BID	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 53
ZINC	20 mg	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 50
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;MALIC ACID;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 44
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 53
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 98
POTASSIUM	20 mmol	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 43
THIAMINE	300 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 45
ASCORBIC ACID;BIOTIN;CYANOCOBALAMIN;FOLIC ACID;NICOTINAMIDE;PANTOTHENIC ACID;PYRIDOXINE;RIBOFLAVIN;THIAMINE	10 mL	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 52
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;MALIC ACID;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	3000 mL	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 48
POTASSIUM	20 mmol	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 47
VITAMINS NOS	1500 mL	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 52
MESALAZINE	1 g	QD	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 50
ADALIMUMAB	80 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 46
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;MALIC ACID;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 47
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 49

POTASSIUM	10 mmol	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 53
SODIUM PHOSPHATE	6 mmol	TID	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 53
ASCORBIC ACID;BIOTIN;CYANOCOBALAMIN;FOLIC ACID;NICOTINAMIDE;PANTOTHENIC ACID;PYRIDOXINE;RIBOFLAVIN;THIAMINE	10 mL	QD	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 52
CHROMIUM;COPPER;IODINE;IRON;MANGANESE;MOLYBDENUM;SELENIUM;SODIUM FLUORIDE;ZINC CHLORIDE	10 mL	QD	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 52
ERGOCALCIFEROL;PHYTOMENADIONE;RETINOL;TOCOPHEROL	10 mL	QD	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 52
CYAMOPSIS TETRAGONOLOBA	1 OTHER: TEASPOON	QID	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 97
LOPERAMIDE	10 mg	OTHER: ON DEMAND	Y-M: 20[redacted] / 50	ONGOING
METHYLPREDNISOLONE	20 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 50
MESALAZINE	2 g	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 97
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 81
URSODEOXYCHOLIC ACID	500 mg	BID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 98
ZINC	20 mg	QD	Y-M: 20[redacted] / 53	ONGOING
GLUCOSE	500 mL	OTHER: 24/H	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 72
HEPARIN	35000 IU	OTHER: 24/H	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 72
RIVAROXABAN	15 mg	BID	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 89

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

Event Description	PHARYNGITIS (VIRAL INFECTION)
Preferred term	ウイルス性咽頭炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 35
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 42): Alanine Aminotransferase: 28 [NOT REPORTED - 55] U/L; Albumin: 31 [34 - 48] G/L; Alkaline Phosphatase: 121 [53 - 128] U/L; Aspartate Aminotransferase: 30 [NOT REPORTED - 40] U/L; Bilirubin: 9 [NOT REPORTED - 20] umol/L; Calcium: 2.1 [2 - 2.6] MMOL/L; Chloride: 90 [95 - 113] MMOL/L; Cholesterol: 3.7 [NOT REPORTED - 5] mmol/L; Creatine Kinase: 104 [NOT REPORTED - 170] U/L; Creatinine: 130 [NOT REPORTED - 115] umol/L; Eosinophils/Leukocytes: 0.5 [NOT REPORTED - 8] %; Glucose: 5 [3.9 - 5.6] MMOL/L; Hematocrit: 0.358 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 121 [140 - 180] G/L; Leukocytes: 14.7 [4 - 10] G/L; Lymphocytes: 1.4 [NOT REPORTED - NOT REPORTED] G/L; Lymphocytes/Leukocytes: 9.6 [20 - 52] %; Monocytes/Leukocytes: 6.3 [2 - 12] %; NPTST159-CRP: 70 [NOT REPORTED - 8] mg/L; NPTST233-GAMMA GLUTAMYLTRANSFERASE: 70 [NOT REPORTED - 65] U/L; NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST300-LACTATDEHYDROGENASE: 225 [NOT REPORTED - 265] U/L; NPTST369-PANCREATIC AMYLASE: 90 [NOT REPORTED - 46] U/L; NPTST390-PHOSPATE: 1.1 [0.8 - 1.5] MMOL/L; Platelets: 514 [150 - 300] G/L; Potassium: 3.2 [3.5 - 5.1] MMOL/L; Protein: 73 [63 - 83] G/L; Sodium: 123 [136 - 144] MMOL/L; Triglycerides: 0.7 [NOT REPORTED - 1.7] mmol/L; Urate: 322 [210 - 430] UMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 43): ABDOMINAL ULTRASOUND: PANCOLITIS

AE Stopped Rx Day	53 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	19 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	VIRAL INFECTION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY

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

Event Description	ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 41
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 42): Alanine Aminotransferase: 28 [NOT REPORTED - 55] U/L; Albumin: 31 [34 - 48] G/L; Alkaline Phosphatase: 121 [53 - 128] U/L; Aspartate Aminotransferase: 30 [NOT REPORTED - 40] U/L; Bilirubin: 9 [NOT REPORTED - 20] umol/L; Calcium: 2.1 [2 - 2.6] MMOL/L; Chloride: 90 [95 - 113] MMOL/L; Cholesterol: 3.7 [NOT REPORTED - 5] mmol/L; Creatine Kinase: 104 [NOT REPORTED - 170] U/L; Creatinine: 130 [NOT REPORTED - 115] umol/L; Eosinophils/Leukocytes: 0.5 [NOT REPORTED - 8] %; Glucose: 5 [3.9 - 5.6] MMOL/L; Hematocrit: 0.358 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 121 [140 - 180] G/L; Leukocytes: 14.7 [4 - 10] G/L; Lymphocytes: 1.4 [NOT REPORTED - NOT REPORTED] G/L; Lymphocytes/Leukocytes: 9.6 [20 - 52] %; Monocytes/Leukocytes: 6.3 [2 - 12] %; NPTST159-CRP: 70 [NOT REPORTED - 8] mg/L; NPTST233-GAMMA GLUTAMYLTRANSFERASE: 70 [NOT REPORTED - 65] U/L; NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST300-LACTATDEHYDROGENASE: 225 [NOT

REPORTED - 265] U/L; NPTST369-PANCREATIC AMYLASE: 90 [NOT REPORTED - 46] U/L; NPTST390-PHOSPATE: 1.1 [0.8 - 1.5] MMOL/L; Platelets: 514 [150 - 300] G/L; Potassium: 3.2 [3.5 - 5.1] MMOL/L; Protein: 73 [63 - 83] G/L; Sodium: 123 [136 - 144] MMOL/L; Triglycerides: 0.7 [NOT REPORTED - 1.7] mmol/L; Urate: 322 [210 - 430] UMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 43): ABDOMINAL ULTRASOUND: PANCOLITIS

AE Stopped Rx Day	53 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	13 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CONSTANT ACTIVITY OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event, Event of Interest - Adjudicated cardiovascular events

Event Description	DEEP VENOUS THROMBOSIS
Preferred term	深部静脈血栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 70 (25 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 70): Alanine Aminotransferase: 49 [NOT REPORTED - 55] U/L; Albumin: 24.6 [34 - 48] G/L; Albumin: 28.4 [34 - 48] G/L; Alkaline Phosphatase: 121 [53 - 128] U/L; Aspartate Aminotransferase: 53 [NOT REPORTED - 40] U/L; Basophils/Leukocytes: 0.2 [NOT REPORTED - 2] %; Calcium: 2.1 [2 - 2.6] MMOL/L; Chloride: 95 [95 - 113] MMOL/L; Cholesterol: 4.7 [NOT REPORTED - 5] mmol/L; Creatine Kinase: 106 [NOT REPORTED - 170] U/L; Creatinine: 124 [NOT REPORTED - 115] umol/L; Eosinophils/Leukocytes: 0.0 [NOT REPORTED - 8] %; Erythrocytes: 4 [4.6 - 6.4] 10^12/L; Glucose: 5.8 [3.9 - 5.6] MMOL/L; Hematocrit: 0.35 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 114 [140 - 180] G/L; Leukocytes: 32.7 [4 - 10] G/L; Lymphocytes: 0.3 [NOT REPORTED - NOT REPORTED] G/L; Lymphocytes/Leukocytes: 1 [20 - 52] %; Monocytes/Leukocytes: 3.8 [2 - 12] %; NPTST159-CRP: 76 [NOT REPORTED - 8] mg/L; NPTST238-GGT: 104 [NOT REPORTED - 65] U/L; NPTST249-GRANULOCYTES: 31.0 [NOT REPORTED - NOT REPORTED] G/L; NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST306-LDH: 442 [NOT REPORTED - 265] U/L; NPTST369-PANCREATIC AMYLASE: 55 [NOT REPORTED - 46] U/L; NPTST391-PHOSPHATE: 1.1 [0.8 - 1.5] MMOL/L; NPTST394-PICT: 60 [NOT REPORTED - NOT REPORTED] sec; NPTST420-QUICK: 113 [81 - 143] %; NPTST510-UREA: 7.2 [2 - 8] MMOL/L; Neutrophils/Leukocytes: 95 [25 - 78] %; Platelets: 365 [150 - 300] G/L; Potassium: 4.7 [3.5 - 5.1] MMOL/L; Protein: 67 [63 - 83] G/L; Sodium: 129 [136 - 144] MMOL/L; Triglycerides: 1.2 [NOT REPORTED - 1.7] mmol/L; Urate: 373 [210 - 430] UMOL/L; [redacted]20[redacted] (RX DAY 71): NPTST394-PICT: 53 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 71 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 93 [NOT REPORTED - NOT REPORTED] sec; [redacted]20[redacted] (RX DAY 72): NPTST394-PICT: 91 [NOT REPORTED - NOT REPORTED] sec; [redacted]20[redacted] (RX DAY 74): Aspartate Aminotransferase: 18 [NOT REPORTED - 40] U/L; Basophils/Leukocytes: 0.2 [NOT REPORTED - 2] %; Bilirubin: 5 [NOT REPORTED - 20] umol/L; Creatinine: 107 [NOT REPORTED - 115] umol/L; Eosinophils/Leukocytes: 0.0 [NOT

REPORTED - 8] %; Erythrocytes: 3.5 [4.6 - 6.4] 10^12/L; Hematocrit: 0.3 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 99 [140 - 180] G/L; Leukocytes: 13.8 [4 - 10] G/L; Lymphocytes: 0.3 [NOT REPORTED - NOT REPORTED] G/L; Lymphocytes/Leukocytes: 1.8 [20 - 52] %; Monocytes/Leukocytes: 3.8 [2 - 12] %; NPTST159-CRP: 68 [NOT REPORTED - 8] mg/L; NPTST238-GGT: 110 [NOT REPORTED - 65] U/L; NPTST249-GRANULOCYTES: 13.0 [NOT REPORTED - NOT REPORTED] G/L; NPTST296-INR: 1.2 [0.9 - 1.1] RATIO; NPTST420-QUICK: 70 [81 - 143] %; NPTST503-TSH: 3.25 [0.25 - 4] MIU/L; Neutrophils/Leukocytes: 94.2 [25 - 78] %; Platelets: 447 [150 - 300] G/L; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Sodium: 136 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 75): Alanine Aminotransferase: 19 [NOT REPORTED - 55] U/L; Alkaline Phosphatase: 85 [53 - 128] U/L; Aspartate Aminotransferase: <10 [NOT REPORTED - 40] U/L; Bilirubin: 4 [NOT REPORTED - 20] umol/L; Creatinine: 106 [NOT REPORTED - 115] umol/L; Erythrocytes: 3.4 [4.6 - 6.4] 10^12/L; Hematocrit: 0.3 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 92 [140 - 180] G/L; Leukocytes: 10.7 [4 - 10] G/L; NPTST238-GGT: 95 [NOT REPORTED - 65] U/L; NPTST296-INR: 1.5 [0.9 - 1.1] RATIO; NPTST420-QUICK: 46 [81 - 143] %; Platelets: 488 [150 - 300] G/L; Sodium: 136 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 76): NPTST159-CRP: 48 [NOT REPORTED - 8] mg/L; [redacted]20[redacted] (RX DAY 78): Albumin: 18.7 [34 - 48] G/L; Creatinine: 91 [NOT REPORTED - 115] umol/L; Erythrocytes: 3.1 [4.6 - 6.4] 10^12/L; Hematocrit: 0.276 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 87 [140 - 180] G/L; Leukocytes: 11.4 [4 - 10] G/L; NPTST159-CRP: 14 [NOT REPORTED - 8] mg/L; NPTST319-MAGNESIUM: 0.8 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 0.9 [0.8 - 1.5] MMOL/L; NPTST510-UREA: 6.2 [2 - 8] MMOL/L; Platelets: 528 [150 - 300] G/L; Sodium: 139 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 79): Albumin: 20.1 [34 - 48] G/L; Creatinine: 94 [NOT REPORTED - 115] umol/L; Erythrocytes: 3.2 [4.6 - 6.4] 10^12/L; Erythrocytes: 584 [150 - 300] 10^12/L; Hematocrit: 0.281 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 87 [140 - 180] G/L; Leukocytes: 12.2 [4 - 10] G/L; NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST319-MAGNESIUM: 0.9 [0.7 - 1.1] MMOL/L; NPTST420-QUICK: 119 [81 - 143] %; NPTST510-UREA: 6.6 [2 - 8] MMOL/L; Potassium: 4 [3.5 - 5.1] MMOL/L; Sodium: 135 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 80): Albumin: 20.5 [34 - 48] G/L; Creatinine: 84 [NOT REPORTED - 115] umol/L; Erythrocytes: 3.2 [4.6 - 6.4] 10^12/L; Erythrocytes: 628 [150 - 300] 10^12/L; Glucose: 5.2 [3.9 - 5.6] MMOL/L; Hematocrit: 0.279 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 86 [140 - 180] G/L; Leukocytes: 14.8 [4 - 10] G/L; NPTST319-MAGNESIUM: 0.9 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 1.0 [0.8 - 1.5] MMOL/L; NPTST510-UREA: 8.0 [2 - 8] MMOL/L; Potassium: 3.7 [3.5 - 5.1] MMOL/L; Sodium: 138 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 81): Albumin: 20.1 [34 - 48] G/L; Calcium: 1.9 [2 - 2.6] MMOL/L; Creatinine: 99 [NOT REPORTED - 115] umol/L; Erythrocytes: 3 [4.6 - 6.4] 10^12/L; Hematocrit: 0.263 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 82 [140 - 180] G/L; Leukocytes: 14.8 [4 - 10] G/L; NPTST319-MAGNESIUM: 0.8 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 0.9 [0.8 - 1.5] MMOL/L; Platelets: 603 [150 - 300] G/L; Potassium: 3.1 [3.5 - 5.1] MMOL/L; Sodium: 139 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 82): Calcium: 1.9 [2 - 2.6] MMOL/L; Creatinine: 86 [NOT REPORTED - 115] mmol/L; NPTST391-PHOSPHATE: 1.0 [0.8 - 1.5] MMOL/L; Potassium: 3.2 [3.5 - 5.1] MMOL/L; Sodium: 139 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 83): NPTST389-PHOPHATE: 0.7 [0.8 - 1.5] MMOL/L; Sodium: 135 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 84): Albumin: 21 [34 - 48] G/L; Calcium: 1.9 [2 - 2.6] MMOL/L; Creatinine: 96 [NOT REPORTED - 115] mmol/L; Erythrocytes: 2.9 [4.6 - 6.4] 10^12/L; Hematocrit: 0.254 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 79 [140 - 180] G/L; Leukocytes: 17.2 [4 - 10] G/L; NPTST159-CRP: 8 [NOT REPORTED - 8] mg/L; NPTST219-FERRITIN: 19 [25 - 330] UG/L; NPTST319-MAGNESIUM: 0.9 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 1.0 [0.8 - 1.5] MMOL/L; Platelets: 570 [150 - 300] G/L; Potassium: 3.3 [3.5 - 5.1] MMOL/L; Sodium: 140 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 86): NPTST223-FOLIC ACID: 10.8 [3 - 20] UG/L; NPTST523-VITAMIN B12: 338 [180 - 900] NG/L; [redacted]20[redacted] (RX DAY 87): Albumin: 20.3 [34 - 48] G/L; Calcium: 1.9 [2 - 2.6] MMOL/L; Creatinine: 90 [NOT REPORTED - 115] umol/L; Erythrocytes: 2.6 [4.6 - 6.4] 10^12/L; Hematocrit: 0.231 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 71 [140 - 180] G/L; Leukocytes: 17.7 [4 - 10] G/L; NPTST159-CRP: 16 [NOT REPORTED - 8] mg/L; NPTST391-PHOSPHATE: 1.0 [0.8 - 1.5] MMOL/L; Platelets: 523 [150 - 300] G/L; Potassium: 4.1 [3.5 - 5.1] MMOL/L; Sodium: 143 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 88): Potassium: 4 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 91): Albumin: 21.1 [34 - 48] G/L; Potassium: 3.4 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 93): NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST420-QUICK: 122 [81 - 143] %; [redacted]20[redacted] (RX DAY 94): Alanine Aminotransferase: 13 [NOT REPORTED - 40] U/L; Albumin: 19.5 [34 - 48] G/L; Alkaline Phosphatase: 62 [53 - 128] U/L; Aspartate Aminotransferase: 16 [NOT REPORTED - 40] U/L; Bilirubin: 5 [NOT REPORTED - 20] umol/L; Calcium: 1.9 [2 - 2.6] MMOL/L; Chloride: 108 [95 - 113] MMOL/L; Creatinine: 86 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 18 [NOT REPORTED - 8] mg/L; NPTST238-GGT: 60 [NOT REPORTED -

65] U/L; NPTST319-MAGNESIUM: 0.8 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 0.7 [0.8 - 1.5] MMOL/L; Potassium: 3.5 [3.5 - 5.1] MMOL/L; Sodium: 138 [136 - 144] MMOL/L; Triglycerides: 0.8 [NOT REPORTED - 1.7] mmol/L; [redacted] (RX DAY 96): NPTST394-PICT: 46 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 29 [NOT REPORTED - NOT REPORTED] sec; [redacted] (RX DAY 97): NPTST394-PICT: 70 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 59 [NOT REPORTED - NOT REPORTED] sec; [redacted] (RX DAY 98): Albumin: 22.2 [34 - 48] G/L; Chloride: 107 [95 - 113] MMOL/L; Creatinine: 97 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 53 [NOT REPORTED - 8] mg/L; NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST391-PHOSPHATE: 1.1 [0.8 - 1.5] MMOL/L; NPTST420-QUICK: 114 [81 - 143] %; Potassium: 3.7 [3.5 - 5.1] MMOL/L; Sodium: 139 [136 - 144] MMOL/L; [redacted] (RX DAY 99): Creatinine: 98 [NOT REPORTED - 115] umol/L; Creatinine: 98 [NOT REPORTED - 115] umol/L; NPTST296-INR: 1.0 [0.9 - 1.1] RATIO; NPTST420-QUICK: 99 [81 - 143] %; NPTST510-UREA: 9.7 [2 - 8] MMOL/L; [redacted] (RX DAY 100): Creatinine: 102 [NOT REPORTED - 102] umol/L; NPTST159-CRP: 173 [NOT REPORTED - 8] mg/L; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Sodium: 141 [136 - 144] MMOL/L; [redacted] (RX DAY 102): Creatinine: 106 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 84 [NOT REPORTED - 8] mg/L; NPTST394-PICT: 34 [NOT REPORTED - NOT REPORTED] sec; Potassium: 3.2 [3.5 - 5.1] MMOL/L; Sodium: 141 [136 - 144] MMOL/L; [redacted] (RX DAY 104): Creatinine: 109 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 201 [NOT REPORTED - 8] mg/L; Potassium: 4.2 [3.5 - 5.1] MMOL/L; [redacted] (RX DAY 105): NPTST296-INR: 1.0 [0.9 - 1.1] RATIO; [redacted] (RX DAY 106): Alanine Aminotransferase: 11 [NOT REPORTED - 11] U/L; Albumin: 13.1 [34 - 48] G/L; Alkaline Phosphatase: 104 [53 - 128] U/L; Aspartate Aminotransferase: 17 [NOT REPORTED - 40] U/L; Bilirubin: 10 [NOT REPORTED - 20] umol/L; Calcium: 1.8 [2 - 2.6] MMOL/L; Creatinine: 123 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 214 [NOT REPORTED - 8] mg/L; NPTST238-GGT: 172 [NOT REPORTED - 65] g/L; NPTST391-PHOSPHATE: 0.8 [0.8 - 1.5] MMOL/L; NPTST394-PICT: 36 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 31 [NOT REPORTED - NOT REPORTED] sec; NPTST420-QUICK: 90 [81 - 143] %; NPTST510-UREA: 5.0 [2 - 8] MMOL/L; Potassium: 3.8 [3.5 - 4.1] MMOL/L; Sodium: 137 [136 - 144] MMOL/L; [redacted] (RX DAY 107): Creatinine: 118 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 112 [NOT REPORTED - 8] mg/L; NPTST296-INR: 1.0 [0.9 - 1.1] RATIO; NPTST394-PICT: 73 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 37 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 52 [NOT REPORTED - NOT REPORTED] sec; NPTST420-QUICK: 84 [81 - 143] %; Potassium: 4 [3.5 - 5.1] MMOL/L; [redacted] (RX DAY 108): NPTST394-PICT: 83 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 77 [NOT REPORTED - NOT REPORTED] sec; [redacted] (RX DAY 109): Creatinine: 115 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 58 [NOT REPORTED - 8] mg/L; NPTST296-INR: 1.0 [0.9 - 1.1] RATIO; NPTST394-PICT: 58 [NOT REPORTED - NOT REPORTED] sec; NPTST420-QUICK: 86 [81 - 143] %; Potassium: 4.5 [3.5 - 5.1] MMOL/L

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SAE Supplemental Procedure

[redacted] (RX DAY 70): ANGIO ULTRASOUND: DEEP LEG THROMBOSIS IN BOTH LEGS; [redacted] (RX DAY 71): TRANSESOPHAGEAL ECHOCARDIOGRAMM: NO RIGHT VENTRICULAR LOAD; [redacted] (RX DAY 74): CT THORAX: CONFIRMATION OF SUBSEGMENTAL LUNG EMBOLISM; [redacted] (RX DAY 78): ECHOCARDIOGRAPHY: NO EVIDENCE OF CARDIOVASCULAR DISEASE; [redacted] (RX DAY 81): ERGOMETERY: REDUCED; [redacted] (RX DAY 93): CAVA UMBRELLA-STENT INSERTION: PREVENTION OF LUNG EMBOLISM

AE Stopped Rx Day	74 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	5 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	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #4: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated cardiovascular events

Event Description	PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 70 (25 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 70): Alanine Aminotransferase: 49 [NOT REPORTED - 55] U/L; Albumin: 24.6 [34 - 48] G/L; Albumin: 28.4 [34 - 48] G/L; Alkaline Phosphatase: 121 [53 - 128] U/L; Aspartate Aminotransferase: 53 [NOT REPORTED - 40] U/L; Basophils/Leukocytes: 0.2 [NOT REPORTED - 2] %; Calcium: 2.1 [2 - 2.6] MMOL/L; Chloride: 95 [95 - 113] MMOL/L; Cholesterol: 4.7 [NOT REPORTED - 5] mmol/L; Creatine Kinase: 106 [NOT REPORTED - 170] U/L; Creatinine: 124 [NOT REPORTED - 115] umol/L; Eosinophils/Leukocytes: 0.0 [NOT REPORTED - 8] %; Erythrocytes: 4 [4.6 - 6.4] 10^12/L; Glucose: 5.8 [3.9 - 5.6] MMOL/L; Hematocrit: 0.35 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 114 [140 - 180] G/L; Leukocytes: 32.7 [4 - 10] G/L; Lymphocytes: 0.3 [NOT REPORTED - NOT REPORTED] G/L; Lymphocytes/Leukocytes: 1 [20 - 52] %; Monocytes/Leukocytes: 3.8 [2 - 12] %; NPTST159-CRP: 76 [NOT REPORTED - 8] mg/L; NPTST238-GGT: 104 [NOT REPORTED - 65] U/L; NPTST249-GRANULOCYTES: 31.0 [NOT REPORTED - NOT REPORTED] G/L; NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST306-LDH: 442 [NOT REPORTED - 265] U/L; NPTST369-PANCREATIC AMYLASE: 55 [NOT REPORTED - 46] U/L; NPTST391-PHOSPHATE: 1.1 [0.8 - 1.5] MMOL/L; NPTST394-PICT: 60 [NOT REPORTED - NOT REPORTED] sec; NPTST420-QUICK: 113 [81 - 143] %; NPTST510-UREA: 7.2 [2 - 8] MMOL/L; Neutrophils/Leukocytes: 95 [25 - 78] %; Platelets: 365 [150 - 300] G/L; Potassium: 4.7 [3.5 - 5.1] MMOL/L; Protein: 67 [63 - 83] G/L; Sodium: 129 [136 - 144] MMOL/L; Triglycerides: 1.2 [NOT REPORTED - 1.7] mmol/L; Urate: 373 [210 - 430] UMOL/L; [redacted]20[redacted] (RX DAY 71): NPTST394-PICT: 53 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 71 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 93 [NOT REPORTED - NOT REPORTED] sec; [redacted]20[redacted] (RX DAY 72): NPTST394-PICT: 91 [NOT REPORTED - NOT REPORTED] sec; [redacted]20[redacted] (RX DAY 74): Aspartate Aminotransferase: 18 [NOT REPORTED - 40] U/L; Basophils/Leukocytes: 0.2 [NOT REPORTED - 2] %; Bilirubin: 5 [NOT REPORTED - 20] umol/L; Creatinine: 107 [NOT REPORTED - 115] umol/L; Eosinophils/Leukocytes: 0.0 [NOT REPORTED - 8] %; Erythrocytes: 3.5 [4.6 - 6.4] 10^12/L; Hematocrit: 0.3 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 99 [140 - 180] G/L; Leukocytes: 13.8 [4 - 10] G/L; Lymphocytes: 0.3 [NOT REPORTED - NOT REPORTED] G/L; Lymphocytes/Leukocytes: 1.8 [20 - 52] %; Monocytes/Leukocytes: 3.8 [2 - 12] %; NPTST159-CRP: 68 [NOT REPORTED - 8] mg/L; NPTST238-GGT: 110 [NOT REPORTED - 65] U/L; NPTST249-GRANULOCYTES: 13.0 [NOT REPORTED - NOT REPORTED] G/L; NPTST296-INR: 1.2 [0.9 - 1.1] RATIO; NPTST420-QUICK: 70 [81 - 143] %; NPTST503-TSH: 3.25 [0.25 - 4] MIU/L; Neutrophils/Leukocytes: 94.2 [25 - 78] %; Platelets: 447 [150 - 300] G/L; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Sodium: 136 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 75): Alanine Aminotransferase: 19 [NOT REPORTED - 55] U/L; Alkaline Phosphatase: 85 [53 - 128] U/L; Aspartate Aminotransferase: <10 [NOT REPORTED - 40] U/L; Bilirubin: 4 [NOT REPORTED - 20] umol/L; Creatinine: 106 [NOT REPORTED - 115] umol/L; Erythrocytes: 3.4 [4.6 - 6.4] 10^12/L; Hematocrit: 0.3 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 92 [140 - 180] G/L; Leukocytes: 10.7 [4 - 10] G/L; NPTST238-GGT: 95 [NOT REPORTED - 65] U/L; NPTST296-INR: 1.5 [0.9 - 1.1] RATIO; NPTST420-QUICK: 46 [81 - 143] %; Platelets: 488 [150 - 300] G/L; Sodium: 136 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 76): NPTST159-CRP: 48 [NOT REPORTED - 8] mg/L; [redacted]20[redacted] (RX DAY 78): Albumin: 18.7 [34 - 48] G/L; Creatinine: 91 [NOT REPORTED - 115] umol/L; Erythrocytes: 3.1 [4.6 - 6.4] 10^12/L; Hematocrit: 0.276 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 87 [140 - 180] G/L; Leukocytes: 11.4 [4 - 10] G/L; NPTST159-CRP: 14 [NOT REPORTED - 8] mg/L; NPTST319-MAGNESIUM: 0.8 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 0.9 [0.8 - 1.5] MMOL/L; NPTST510-

UREA: 6.2 [2 - 8] MMOL/L; Platelets: 528 [150 - 300] G/L; Sodium: 139 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 79): Albumin: 20.1 [34 - 48] G/L; Creatinine: 94 [NOT REPORTED - 115] umol/L; Erythrocytes: 3.2 [4.6 - 6.4] 10^12/L; Erythrocytes: 584 [150 - 300] 10^12/L; Hematocrit: 0.281 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 87 [140 - 180] G/L; Leukocytes: 12.2 [4 - 10] G/L; NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST319-MAGNESIUM: 0.9 [0.7 - 1.1] MMOL/L; NPTST420-QUICK: 119 [81 - 143] %; NPTST510-UREA: 6.6 [2 - 8] MMOL/L; Potassium: 4 [3.5 - 5.1] MMOL/L; Sodium: 135 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 80): Albumin: 20.5 [34 - 48] G/L; Creatinine: 84 [NOT REPORTED - 115] umol/L; Erythrocytes: 3.2 [4.6 - 6.4] 10^12/L; Erythrocytes: 628 [150 - 300] 10^12/L; Glucose: 5.2 [3.9 - 5.6] MMOL/L; Hematocrit: 0.279 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 86 [140 - 180] G/L; Leukocytes: 14.8 [4 - 10] G/L; NPTST319-MAGNESIUM: 0.9 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 1.0 [0.8 - 1.5] MMOL/L; NPTST510-UREA: 8.0 [2 - 8] MMOL/L; Potassium: 3.7 [3.5 - 5.1] MMOL/L; Sodium: 138 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 81): Albumin: 20.1 [34 - 48] G/L; Calcium: 1.9 [2 - 2.6] MMOL/L; Creatinine: 99 [NOT REPORTED - 115] umol/L; Erythrocytes: 3 [4.6 - 6.4] 10^12/L; Hematocrit: 0.263 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 82 [140 - 180] G/L; Leukocytes: 14.8 [4 - 10] G/L; NPTST319-MAGNESIUM: 0.8 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 0.9 [0.8 - 1.5] MMOL/L; Platelets: 603 [150 - 300] G/L; Potassium: 3.1 [3.5 - 5.1] MMOL/L; Sodium: 139 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 82): Calcium: 1.9 [2 - 2.6] MMOL/L; Creatinine: 86 [NOT REPORTED - 115] mmol/L; NPTST391-PHOSPHATE: 1.0 [0.8 - 1.5] MMOL/L; Potassium: 3.2 [3.5 - 5.1] MMOL/L; Sodium: 139 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 83): NPTST389-PHOPHATE: 0.7 [0.8 - 1.5] MMOL/L; Sodium: 135 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 84): Albumin: 21 [34 - 48] G/L; Calcium: 1.9 [2 - 2.6] MMOL/L; Creatinine: 96 [NOT REPORTED - 115] mmol/L; Erythrocytes: 2.9 [4.6 - 6.4] 10^12/L; Hematocrit: 0.254 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 79 [140 - 180] G/L; Leukocytes: 17.2 [4 - 10] G/L; NPTST159-CRP: 8 [NOT REPORTED - 8] mg/L; NPTST219-FERRITIN: 19 [25 - 330] UG/L; NPTST319-MAGNESIUM: 0.9 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 1.0 [0.8 - 1.5] MMOL/L; Platelets: 570 [150 - 300] G/L; Potassium: 3.3 [3.5 - 5.1] MMOL/L; Sodium: 140 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 86): NPTST223-FOLIC ACID: 10.8 [3 - 20] UG/L; NPTST523-VITAMIN B12: 338 [180 - 900] NG/L; [redacted]20[redacted] (RX DAY 87): Albumin: 20.3 [34 - 48] G/L; Calcium: 1.9 [2 - 2.6] MMOL/L; Creatinine: 90 [NOT REPORTED - 115] umol/L; Erythrocytes: 2.6 [4.6 - 6.4] 10^12/L; Hematocrit: 0.231 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 71 [140 - 180] G/L; Leukocytes: 17.7 [4 - 10] G/L; NPTST159-CRP: 16 [NOT REPORTED - 8] mg/L; NPTST391-PHOSPHATE: 1.0 [0.8 - 1.5] MMOL/L; Platelets: 523 [150 - 300] G/L; Potassium: 4.1 [3.5 - 5.1] MMOL/L; Sodium: 143 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 88): Potassium: 4 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 91): Albumin: 21.1 [34 - 48] G/L; Potassium: 3.4 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 93): NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST420-QUICK: 122 [81 - 143] %; [redacted]20[redacted] (RX DAY 94): Alanine Aminotransferase: 13 [NOT REPORTED - 40] U/L; Albumin: 19.5 [34 - 48] G/L; Alkaline Phosphatase: 62 [53 - 128] U/L; Aspartate Aminotransferase: 16 [NOT REPORTED - 40] U/L; Bilirubin: 5 [NOT REPORTED - 20] umol/L; Calcium: 1.9 [2 - 2.6] MMOL/L; Chloride: 108 [95 - 113] MMOL/L; Creatinine: 86 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 18 [NOT REPORTED - 8] mg/L; NPTST238-GGT: 60 [NOT REPORTED - 65] U/L; NPTST319-MAGNESIUM: 0.8 [0.7 - 1.1] MMOL/L; NPTST391-PHOSPHATE: 0.7 [0.8 - 1.5] MMOL/L; Potassium: 3.5 [3.5 - 5.1] MMOL/L; Sodium: 138 [136 - 144] MMOL/L; Triglycerides: 0.8 [NOT REPORTED - 1.7] mmol/L; [redacted]20[redacted] (RX DAY 96): NPTST394-PICT: 46 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 29 [NOT REPORTED - NOT REPORTED] sec; [redacted]20[redacted] (RX DAY 97): NPTST394-PICT: 70 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 59 [NOT REPORTED - NOT REPORTED] sec; [redacted]20[redacted] (RX DAY 98): Albumin: 22.2 [34 - 48] G/L; Chloride: 107 [95 - 113] MMOL/L; Creatinine: 97 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 53 [NOT REPORTED - 8] mg/L; NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST391-PHOSPHATE: 1.1 [0.8 - 1.5] MMOL/L; NPTST420-QUICK: 114 [81 - 143] %; Potassium: 3.7 [3.5 - 5.1] MMOL/L; Sodium: 139 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 99): Creatinine: 98 [NOT REPORTED - 115] umol/L; Creatinine: 98 [NOT REPORTED - 115] umol/L; NPTST296-INR: 1.0 [0.9 - 1.1] RATIO; NPTST420-QUICK: 99 [81 - 143] %; NPTST510-UREA: 9.7 [2 - 8] MMOL/L; [redacted]20[redacted] (RX DAY 100): Creatinine: 102 [NOT REPORTED - 102] umol/L; NPTST159-CRP: 173 [NOT REPORTED - 8] mg/L; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Sodium: 141 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 102): Creatinine: 106 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 84 [NOT REPORTED - 8] mg/L; NPTST394-PICT: 34 [NOT REPORTED - NOT REPORTED] sec; Potassium: 3.2 [3.5 - 5.1] MMOL/L; Sodium: 141 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 104): Creatinine: 109 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 201 [NOT REPORTED - 8] mg/L; Potassium: 4.2 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY

105): NPTST296-INR: 1.0 [0.9 - 1.1] RATIO; [redacted]20[redacted] (RX DAY 106): Alanine Aminotransferase: 11 [NOT REPORTED - 11] U/L; Albumin: 13.1 [34 - 48] G/L; Alkaline Phosphatase: 104 [53 - 128] U/L; Aspartate Aminotransferase: 17 [NOT REPORTED - 40] U/L; Bilirubin: 10 [NOT REPORTED - 20] umol/L; Calcium: 1.8 [2 - 2.6] MMOL/L; Creatinine: 123 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 214 [NOT REPORTED - 8] mg/L; NPTST238-GGT: 172 [NOT REPORTED - 65] g/L; NPTST391-PHOSPHATE: 0.8 [0.8 - 1.5] MMOL/L; NPTST394-PICT: 36 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 31 [NOT REPORTED - NOT REPORTED] sec; NPTST420-QUICK: 90 [81 - 143] %; NPTST510-UREA: 5.0 [2 - 8] MMOL/L; Potassium: 3.8 [3.5 - 4.1] MMOL/L; Sodium: 137 [136 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 107): Creatinine: 118 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 112 [NOT REPORTED - 8] mg/L; NPTST296-INR: 1.0 [0.9 - 1.1] RATIO; NPTST394-PICT: 73 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 37 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 52 [NOT REPORTED - NOT REPORTED] sec; NPTST420-QUICK: 84 [81 - 143] %; Potassium: 4 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 108): NPTST394-PICT: 83 [NOT REPORTED - NOT REPORTED] sec; NPTST394-PICT: 77 [NOT REPORTED - NOT REPORTED] sec; [redacted]20[redacted] (RX DAY 109): Creatinine: 115 [NOT REPORTED - 115] umol/L; NPTST159-CRP: 58 [NOT REPORTED - 8] mg/L; NPTST296-INR: 1.0 [0.9 - 1.1] RATIO; NPTST394-PICT: 58 [NOT REPORTED - NOT REPORTED] sec; NPTST420-QUICK: 86 [81 - 143] %; Potassium: 4.5 [3.5 - 5.1] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 70): ANGIO ULTRASOUND: DEEP LEG THROMBOSIS IN BOTH LEGS; [redacted]20[redacted] (RX DAY 71): TRANSESOPHAGEAL ECHOCARDIOGRAMM: NO RIGHT VENTRICULAR LOAD; [redacted]20[redacted] (RX DAY 74): CT THORAX: CONFIRMATION OF SUBSEGMENTAL LUNG EMBOLISM; [redacted]20[redacted] (RX DAY 78): ECHOCARDIOGRAPHY: NO EVIDENCE OF CARDIOVASCULAR DISEASE; [redacted]20[redacted] (RX DAY 81): ERGOMETERY: REDUCED; [redacted]20[redacted] (RX DAY 93): CAVA UMBRELLA-STENT INSERTION: PREVENTION OF LUNG EMBOLISM

AE Stopped Rx Day	74 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はスイスの 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，咽頭炎（ウイルス感染）及び潰瘍性大腸炎の事象を発現した。関連する病歴は，元喫煙者（1 日 0.5 箱を 15 年間），潰瘍性大腸炎，腎障害，副腎機能不全及び元飲酒者（1 日 2 杯未満）であった。

Event 1 及び 2 の臨床経過：

投与35日後＊　，被験者は咽頭炎（ウイルス感染）を発現した。投与41日後＊　，被験者は潰瘍性大腸炎を発現した。投与53日後＊　，咽頭炎（ウイルス感染）及び潰瘍性大腸炎は消失した。

投与42日後＊　，被験者は潰瘍性大腸炎の悪化（1 日に 25–30 回の血性下痢の発現）及び咽頭炎があり，入院した。被験者は喉の痛みを訴えたが，無治療で 5 日後に消失した。被験者はステロイドの静脈内投与に切り替えられ，病状は改善した。投与53日後＊　，被験者は退院した。

投与された薬剤は，salofalk，ソル・メドロール，zink verla，塩化カリウム，phoscaps，prednison 及び imodium であった。

Causality for ABT-494 (Blinded)

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1)　Viral pharyngitis (10047473)　(Viral pharyngitis (10047473))　[v.21.0]　[10047473]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2)　Ulcerative colitis (10045365)　(Colitis ulcerative (10009900))　[v.21.0]　[10045365]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of PHARYNGITIS (VIRAL INFECTION)

- Investigator: viral infection

- AbbVie: VIRAL PHARYNGITIS IS COMMON IN THE GENERAL POPULATION.

Event of ULCERATIVE COLITIS

- Investigator: Constant activity of ulcerative colitis

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Pancolitis

[redacted] **20[redacted] ALBUMIN:** 31 G/L (normal 34 to 48)

[redacted] **20[redacted] CHLORIDE:** 90 MMOL/L (normal 95 to 113)

[redacted] **20[redacted] CREATININE:** 130 MMOL/L (normal <115)

[redacted] **20[redacted] CRP:** 70 MG/L (normal <8)

[redacted] **20[redacted] GAMMA GLUTAMYLTRANSFERASE:** 70 U/L (normal <65)

[redacted] **20[redacted] HEMATOCRIT:** 0.358 % (normal 0.40 to 10.0)

[redacted] **20[redacted] HEMOGLOBIN:** 121 G/L (normal 140 to 180)

[redacted] **20[redacted] INR:** 0.9 % (normal 0.9 to 1.1)

[redacted] **20[redacted] LYMPHOCYTES:** 9.6 % (normal 20 to 52)

[redacted] **20[redacted] PANCREATIC AMYLASE:** 90 U/L (normal <46)

[redacted] **20[redacted] PLATELET COUNT:** 514 G/L (normal 150 to 300)

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

[redacted] **20[redacted] SODIUM:** 123 MMOL/L (normal 136 to 144)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 14.7 G/L (normal 4 to 10)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はスイスの 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，肺塞栓症及び深部静脈血栓症の事象を発現した。関連する病歴は，元喫煙者（1 日 0.5 箱を 15 年間），潰瘍性大腸炎（広範囲な潰瘍性大腸炎／全大腸炎型），慢性腎不全（GFR 区分：G3A，蛋白尿区分：A1），腎障害，副腎機能不全及び元飲酒者（1 日 2 杯未満）であった。

Event3 及び 4 の臨床経過：

投与70日後＊　，被験者は肺塞栓症及び深部静脈血栓症を発現した。投与74日後＊　，肺塞栓症及び深部静脈血栓症は消失した。

本事象発現時，被験者は治験薬投与中止後 30 日間の観察期間中であった。投与70日後＊　，被験者は息切れがあり，痛みを伴うふくらはぎの腫脹が見られた。被験者は 50 メートル以上の距離を歩くことができなかった。被験者は病院を受診し，緊急の血管超音波検査で両足に血栓症が確認された。被験者は，同日入院した。治験責任医師によると，被験者の危険因子は，重症の大腸炎及び炎症，体液喪失，仰臥位での安静患者であること，並びに高用量ステロイドの投与であった。投与74日後＊　，胸部 CT スキャン検査で亜区域性の肺塞栓症と診断された。投与77日後＊　，被験者は発作性及び頻拍性の心房細動を発現したが，治験責任医師は非重篤と判断した。このため，被験者は concor 及び torem を投与された。投与93日後＊　，被験者は大静脈フィルターの設置を受けたが，合併症は認められなかった。

退院時サマリーより：

最も重症な難治性の大腸炎により，この被験者の治験は早期に中止された。　投与42日後＊から 投与53日後＊までの間，大腸炎の急な再燃に伴って入院し体を動かせない状態であったことが，深部静脈血栓症及び肺塞栓症を引き起こした可能性が高いと病院の医師は推測しており，既知の低アルブミン血症や基礎疾患（潰瘍性大腸炎）が更に血栓形成作用を及ぼした可能性があるとした。肺塞栓症及び深部静脈血栓症発症前の 14 日間で，被験者の体重は 2 kg 減少した。また，

NYHA 心機能分類が II–III の労作性呼吸困難，白濁した分泌物を伴う咳嗽，断続的な腹痛，右脚の腫脹，及び 1 日 1 回の周期的な液状便が見られた。頭痛や浮動性めまいはなく，発熱や寝汗もなく，胸痛や排尿障害も見られなかった。投与70日後＊　　，被験者は朝から右脚に痛み，腫脹及び圧迫感を感じ，救急治療室を受診した。被験者は，通常歩行時にすでに呼吸困難感があった。診察の結果，右下肢はびまん性の腫脹及び硬化が見られ，触診ではびまん性の痛みがあり，皮下静脈はしっかりと触知できた。左下肢に腫脹の徴候は見られず，触診では痛みもなく，柔らかかった。肢端の血管領域は左右対称に温かく，末梢の塞栓症や皮膚の栄養障害の徴候はなく，各側の再毛細血管化の時間も正常であった。CT スキャン検査が行われ，肺塞栓症が疑われるレベル 3 の両側下肢静脈の血栓症と診断された。

本事象に対する治療は，抗凝固療法及び大腿部の長さの弾性包帯及びストッキングの着用（クラス II）であった。更に NYHA 心機能分類が II–III の労作性呼吸困難に関して，病院の医師は更なる肺塞栓症を想定し，ヘパリンによる完全な抗凝固療法を開始した。それ以外の血行動態は安定しており，投与71日後＊　　に行われた経胸壁心エコー検査では，右心の負担は見られなかった。そのため，肺塞栓症を検出するための CT スキャン検査は経過観察中にのみ行われ，右下葉に亜区域性の肺塞栓症が見られたが，右心負担の徴候は見られなかった。　　投与77日後＊，被験者は発作性及び頻脈性の心房細動を発現した。胸部及び腹部 CT スキャン検査では，悪性腫瘍の徴候は認められなかった。経過観察中にヘパリン治療を中止し，代わりにイグザレルト 15 mg を 1 日 2 回，最初の 3 週間に投与することとした。更に，クラス II の圧迫ストッキングが処方され，入院中にすでに着用していた。3 週間後，イグザレルトの投与量を 1 日 20 mg に減量した。予定していた結腸切除術のため，リバーロキサバンを再びヘパリンに変更した。更に，投与93日後＊，血栓塞栓症予防のため，結腸切除術の術前に大静脈フィルターを挿入した。

入院時の白血球数が 32 g/L と高値であり，現在ヒュミラで治療中であるが，便の回数が 1 日 10 回以上の下痢が続いていたため，内科で深部静脈血栓症及び肺塞栓症の初期治療を行った後，消化器内科に転科した。CT スキャン検査では，穿孔の形跡を伴わない回結腸炎及び膿瘍を疑う体液の貯留が見られた。超音波検査では汎大腸炎の徴候が見られた。これらの報告を総合的に判断すると，難治性の経過で悪性腫瘍のリスクがあり，更に原発性硬化性胆管炎の可能性も指摘されていることから（また，内視鏡検査の選択肢が限られる最も重症な大腸炎であることから），前回の入院時と同様に，被験者には結腸切除術の外科的治療法を再考することが推奨された。被験者は結腸切除術に前向きであった。また，今回の入院では，腹部外科のクリニックからの医師らとの間で何度か学際的な話し合いが行われ，被験者は結腸切除術を受けることを決めた。術前の準備として，低アルブミン血症を伴う栄養失調の臨床的徴候及び検査所見が見られたため，非経口での補完的な栄養補給が行われた。投与98日後＊　　，最終手段として回腸瘻造設を伴う腹腔鏡下結腸直腸切除術が行われ，合併症もなく終了した。術後の監視は，集中治療室で常に行われた。ステロイドの長期投与による副腎機能不全は既に認知されているため，手術前後に予定通りヒドロコルチゾンによる予防的治療が行われた。被験者は安定状態であっ

たため，投与99日後＊　　に一般外科病棟に転棟できた。リスク因子，すなわちレベル 3 の深部静脈血栓症及び肺塞栓症の既往を考慮し，術後 3 日目に低分子ヘパリンによる治療を治療用量以下の用量で再開した。そして，ヘパリンを治療用量まで増量した後，イグザレルトに切り替えた。手術中に挿入したドレーンの除去は予定通り行われた。炎症マーカーの上昇が見られたため，投与104日後＊ に腹部 CT スキャン検査を実施した。麻痺による小腸通過遅延を伴う回腸炎と診断された。組織学的には悪性腫瘍は確認できなかった。投与106日後＊　　に大静脈フィルターを除去した。通常の食事への移行は良好であった。整腸剤を使用していても，ストーマからの排出量は最大 2000 mL と高水準であった（ハイアウトプットストーマ）。薬剤を imodium から tinctura opii へ切り替え，ストーマの出力を適切なレベルまで下げることができた。投与116日後＊　　，被験者は全身状態が良好で，傷の痛みもなく，リハビリテーションクリニックに転院した。

投与された薬剤は，イグザレルト，torem，liquemin 及び concor であった。

The patient's past medications include:

CICLOSPORIN for ULCERATIVE COLITIS ([redacted])

CIPROXIN for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

AZATHIOPRIN for ULCERATIVE COLITIS ([redacted])

SPIRICORT forULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

TACROLIMUS for ULCERATIVE COLITIS ([redacted])

HYDROCORTISONE for SECONDARY ADRENOCORTICAL INSUFFICIENCY ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

DE-URSIL for PHARYNGITIS ([redacted])

CLEXANE for THROMBOSIS PROPHYLAXIS ([redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted])

SOLU-MEDROL for FLARE OF ULCERATIVE COLITIS ([redacted])

ADDAVEN for MALNUTRITION DUE TO WORSENING OF UC and MALNUTRITION DUE TO WORSENING OF UC ([redacted])

Causality for ABT-494 (Blinded)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.21.0] [10037377]

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

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

Dechallenge: Not Applicable

2) Deep vein thrombosis (10051055) (Deep vein thrombosis (10051055)) [v.21.0] [10051055]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of PULMONARY EMBOLISM

- Investigator: Not applicable.

- AbbVie: Lack of temporal association. Study drug discontinued more than 3 weeks prior to the onset of the event.

Event of DEEP VENOUS THROMBOSIS

- Investigator: Not applicable

- AbbVie: Lack of temporal association. Study drug discontinued more than 3 weeks prior to the onset of the event.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 49 U/L (normal <55)

[redacted] **20[redacted] ALBUMIN:** 28.4 G/L (normal 34 to 48)

[redacted] **20[redacted] ALBUMIN:** 18.7 G/L (normal 34 to 48)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 121 U/L (normal 53 to 128)

[redacted] **20[redacted] ANGIO ULTRASOUND:** deep leg thrombosis in both legs

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 53 MCMOL/L (normal <40)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 18 MCMOL/L (normal <40)

[redacted] **20[redacted] BLOOD PRESSURE:** 115/77 mmHg

[redacted] **20[redacted] BODY TEMPERATURE:** 37 Degrees C

[redacted] **20[redacted] CALCIUM:** 2.1 MMOL/L (normal 2.0 to 2.6)

[redacted] **20[redacted] CHEST AND ABDOMEN CT WITH IV CONTRAST MEDIA:** Subsegmental pulmonary embolism of the left lower lobe with suspected onset of small volume hemorrhagic infarction subpleural posterobasal on the right side. No signs of right ventricular congestion. Ileocolitis due to known ulcerative colitis with primary reactive abdominopelvic lymphadenopathy but no evidence for a perforation and no fluid retention possibly due to an abscess. Thrombosis of the femoralis vein on the right side.

[redacted] **20[redacted] CHEST AND ABDOMEN CT WITH IV CONTRAST MEDIA:** Subsegmental pulmonary embolism of the left lower lobe with suspected onset of small volume hemorrhagic infarction subpleural posterobasal on the right side. No signs of right ventricular congestion. Ileocolitis due to known ulcerative colitis with primary reactive abdominopelvic lymphadenopathy but no evidence for a perforation and no fluid retention possibly due to an abscess. Thrombosis of the femoralis vein on the right side.

[redacted] **20[redacted] CHEST X-RAY:** Compared to previous examination on [redacted] 20[redacted]. History of placement of a central venous catheter jugular right side with projection of the catheter tip on the V. cava superior. No evidence for pneumothorax. Slim heart and mediastinum. Stationary enhanced interstitial lung structure and slightly enlarged lung volume. No pneumonic infiltration. No pleura effusion. Unchanged obliterated recessus phrenicocostales dorsales.

[redacted] **20[redacted] CHLORIDE:** 95 MMOL/L (normal 95 to 113)

[redacted] 20[redacted] **CREATININE:** 124 MCMOL/L (normal <115)

[redacted] 20[redacted] **CREATININE:** 107 MCMOL/L (normal <115)

[redacted] 20[redacted] **CREATININE KINASE:** 106 U/L (normal <170)

[redacted] 20[redacted] **CT ABDOMEN:** An ileitis combined with small intestinal passage delay due to paralysis was diagnosed. Histologically, no malignancy could be found.

[redacted] 20[redacted] **CT THORAX:** Confirmation of subsegmental lung embolism. Subsegmental pulmonary embolism of left lower lobe with suspected onset of small volume hemorrhagic infarction subpleural posterobasal on the right side. No signs of right ventricular congestion.

[redacted] 20[redacted] **DUPLEX SONOGRAPHY:** -RIGHT: - Long segment thrombosis of muscle veins, V. fibularis and V. tibialis posterior, V. poplitea as well as V. femoralis superficialis up to and including V. femoralis communis distal to the intersection (duplex [redacted].[redacted].20[redacted]) -LEFT: -M. soleus-thrombosis, proximal thrombosis of V. fibularis and V. tibialis posterior, thrombosis of V. poplitea, partial thrombosis of doubly disposed V. femoralis superficialis, complete thrombosis of V. femoralis communis just under the area of the intersection (duplex [redacted] 20[redacted])

[redacted] 20[redacted] **ECG:** Normal sinus rhythm, normal ECG.

[redacted] 20[redacted] **ECHOCARDIOGRAPHY:** no evidence of cardiovascular disease

[redacted] 20[redacted] **ECHOCARDIOGRAPHY:** Left ventricle of normal dimension with globally normal systolic function without indication of regional motility disturbances (LVEF approximately 60%, visually estimated). Normal diastolic function. Normal right ventricular dimension and function. No direct indications for a relevant pulmonary pressure increase. No relevant heart valve disease. Both atria of normal dimension.

[redacted] 20[redacted] **ERGOMETRY:** Cycle ergometry, ramp protocol 35-110 87 Watt done (65.9% target, 6.9 METs) during 5:30 min. Heart frequency elevated from 81/min to 152/min (65.9% target). Blood pressure systolic elevated from 96 mmHg to 171 mmHg. Maximal DP 25992, DPF 3.3. Exercise aborted due to dyspnea and tiredness of the legs. No angina pectoris, no dizziness, occasional vesicular extra systoles without elevation upon strain. During exercise no ischemia-specific ECG-changes. SpO2 at rest: 100%, during exercise: 98% Evaluation: No findings regarding an ischemia. Normal circular flow. Reduced performance with 87 Watt (65.9% target) or 6.9 METs.

[redacted] 20[redacted] **FOCUSED SONOGRAPHY:** Normal size proportion LV/RV >1. No pathological D-sign. No evidence of a relevant TI. Visually normal TAPSE. V. cava empty. Therefore, no evidence of a hemodynamically relevant right heart burden.

[redacted] 20[redacted] **GGT:** 104 U/L (normal <65)

[redacted] 20[redacted] **HEART RATE:** 131 /min

[redacted] 20[redacted] **INR:** 0.9 no units, ratio (normal 0.9 to 1.1)

[redacted] 20[redacted] **INR:** 1.2 no units, ratio (normal 0.9 to 1.1)

[redacted] **20[redacted] INR:** 1.5 no units, ratio (normal 0.9 to 1.1)

[redacted] **20[redacted] INR:** 0.9 no units, ratio (normal 0.9 to 1.1)

[redacted] **20[redacted] INR:** 1.0 no units, ratio (normal 0.9 to 1.1)

[redacted] **20[redacted] LDH:**442 U/L (normal <265)

[redacted] **20[redacted] OVERVIEW OF ABDOMEN, LYING A.-P./LEFT-SIDED POSITION:** In left-sided position, scattered gas-fluid level formations in the area of the cecal pole and the descending colon as a sign of a slight intestinal passage disorder with known ileocolitis. No severe passage disorder of a higher grade nor any evidence for a hollow organ perforation. Contrast medium in the bladder from the examination on the previous day. Visible basal lung and bone structures are normal.

[redacted] **20[redacted] PANCREATIC AMYLASE:** 55 U/L (normal <46)

[redacted] **20[redacted] PICT:** 60 SEC

[redacted] **20[redacted] PICT:** 71 SEC

[redacted] **20[redacted] PICT:** 91 SEC

[redacted] **20[redacted] PICT:** 29 SEC

[redacted] **20[redacted] PICT:** 59 SEC

[redacted] **20[redacted] PICT:** 34 SEC

[redacted] **20[redacted] PICT:** 31 SEC

[redacted] **20[redacted] PICT:** 73 SEC

[redacted] **20[redacted] PICT:** 83 SEC

[redacted] **20[redacted] PICT:** 58 SEC

[redacted] **20[redacted] POTASSIUM:** 4.7 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] PROTEIN:** 67 G/L (normal 63 to 83)

[redacted] **20[redacted] QUICK:** 113 % (normal 81 to 143)

[redacted] **20[redacted] QUICK:** 70 % (normal 81 to 143)

[redacted] **20[redacted] QUICK:** 86 % (normal 81 to 143)

[redacted] **20[redacted] SO2:** 99 %

[redacted] **20[redacted] SODIUM:** 129 MMOL/L (normal 136 to 144)

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

[redacted] **20[redacted] SONOGRAPHY:** No evidence of any abdominal masses, however, examination conditions were limited. 1. Pancolitis: Pathological intestinal wall thickening, total colon mucosa thickened (4-5 mm) with accentuated long wall thickening of up to 5 mm in sigma. 2. Accentuated non-dilated biliary tract in both liver segments (previously known) due to PSC – slim DHC. 3. Narrowed kidney parenchyma on both sides.

[redacted] **20[redacted] TRANSESOPHAGEAL ECHOCARDIOGRAM:** no right ventricular load

[redacted] **20[redacted] TRANSTHORACIC ECHOCARDIOGRAPHY:** Left ventricle of normal dimension with normal systolic function without signs of regional motility disturbance. (LVEF about 60%, visual estimate). Normal diastolic function. Normal right ventricular dimension and function. No indirect evidence for relevant pulmonary presre elevation. No relevant valve diseases. Both atria of normal dimension.

[redacted] **20[redacted] UREA:** 7.2 MMOL/L (normal 2 to 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
出血性膀胱炎	X			X

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

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
OSTEOPOROSIS	NOT REPORTED
OTHER: CHOLESTASIS PARAMETER ELEVATED	20[redacted]
OTHER: HETEROZYGOTE MUTATION OF THE TPMT (THIOPURINETHYLTRANSFERASE)	20[redacted]
OTHER: INTERMITTANT WITH SPONTANEOUS HEALING, 3 SMALL UNSPECIFIC RED SPOTS	20[redacted]
OTHER: MENOPAUSE	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 30 mg	30	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
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
PREDNISONE	100 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	TID	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
CALCIUM CARBONATE;COLECALCIFEROL	1 g	QD	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
GOLIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
BUDESONIDE	40 mg	QD	Y-M: 20[redacted]
TACROLIMUS	4 mg	BID	Y-M: 20[redacted]
MESALAZINE	2 g	QD	Y-M: 20[redacted] / -104
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -5
HYOSCINE	10 mg	OTHER: ON DEMAND	Y: 20[redacted]
ANTIDIARRHEAL MICROORGANISMS	10 /20 OTHER: N.A.	BID	Y: 20[redacted]
CURCUMA LONGA	2 g	BID	Y: 20[redacted]
DENOSUMAB	60 mg	OTHER: SIX-MONTHLY	Y: 20[redacted]
LOPERAMIDE	ON DEMAND OTHER: UNKNOWN	OTHER: ON DEMAND	Y: 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
MESALAZINE	1 g	TID	Y-M: 20[redacted]	ONGOING
CALCIUM CARBONATE;COLECALCIFEROL	1 g	QD	Y-M: 20[redacted]	ONGOING
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -5	Y-M: 20[redacted] / -4

CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;MALIC ACID;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	OTHER: 24H/D	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 14
METAMIZOLE	40 gtt	OTHER: ON DEMAND	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 13
SULFAMETHOXAZOLE;TRIMETHOPRIM	800/160 mg	BID	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 16
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 14
HYOSCINE	10 mg	OTHER: ON DEMAND	Y: 20[redacted]	ONGOING
ANTIDIARRHEAL MICROORGANISMS	10 /20 OTHER: N.A.	BID	Y: 20[redacted]	ONGOING
CURCUMA LONGA	2 g	BID	Y: 20[redacted]	Y-M: 20[redacted] / 85
DENOSUMAB	60 mg	OTHER: SIX-MONTHLY	Y: 20[redacted]	ONGOING
LOPERAMIDE	ON DEMAND OTHER: UNKNOWN	OTHER: ON DEMAND	Y: 20[redacted]	ONGOING

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

Event Description	HEMORAGIC CYSTITIS
Preferred term	出血性膀胱炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 12
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 12): Alanine Aminotransferase: 16 [NOT REPORTED - 55] U/L; Albumin: 36.4 [34 - 48] G/L; Alkaline Phosphatase: 130 [42 - 98] U/L; Aspartate Aminotransferase: 26 [NOT REPORTED - 40] U/L; Bilirubin: NEG [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Bilirubin: 7 [NOT REPORTED - 20] umol/L; Calcium: 2.3 [2 - 2.6] MMOL/L; Chloride: 101 [95 - 113] MMOL/L; Cholesterol: 5.5 [NOT REPORTED - 5] mmol/L; Creatine Kinase: 113 [NOT REPORTED - 145] U/L; Creatinine: 60 [NOT REPORTED - 95] umol/L; Erythrocytes: 4.2 [4.2 - 5.4] 10^12/L; Glucose: NORM [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: 5.7 [3.9 - 5.6] MMOL/L; Hematocrit: 0.364 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: +++ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 117 [120 - 160] G/L; Ketones: NEG [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 13.3 [4 - 10] G/L; Leukocytes: + [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST159-CRP: 6 [NOT REPORTED - 8] mg/L; NPTST238-GGT: 110 [NOT REPORTED - 35] U/L; NPTST296-INR: 0.9 [0.9 - 1.1] RATIO; NPTST306-LDH: 203 [NOT REPORTED - 265] U/L; NPTST368-PANCREAS AMYLASE: 17 [NOT REPORTED - 46] U/L; NPTST391-PHOSPHATE: 1.3 [0.8 - 1.5] MMOL/L; NPTST420-QUICK: 129 [81 - 143] %; NPTST510-UREA: 221 [150 - 360] UMOL/L; Nitrite: NEG [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 417 [150 - 300] G/L; Potassium: 3.6 [3.5 - 5.1] MMOL/L; Protein: ++ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 66 [63 - 83] G/L; Sodium: 135 [136 - 144] MMOL/L; Specific Gravity: 1.015 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Triglycerides: 1.1 [NOT REPORTED - 1.7] mmol/L; Urobilinogen: NORM [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; pH:

6.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 13): Erythrocytes: 4.2 [4.2 - 5.4] 10^12/L; Hematocrit: 0.355 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 118 [120 - 150] G/L; Platelets: 387 [150 - 300] G/L; Urobilinogen: NORMAL [NOT REPORTED - NOT REPORTED] NORMAL

Microbiology

[redacted]20[redacted] (RX DAY 12): URINE NPTST518-URINE CULTURE: POSITIVE-E-COLI

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 12): BLADDER IRRIGATION: THE CATHETER WAS REMOVED ON [redacted]-20[redacted] AFTER POSITIVE RESPONSE TO THE IRRIGATION AND ORAL ANTIBIOTICS.; ECG: NORMAL FINDINGS; TEMPERATURE MEASUREMENT: 37.4 C 39.0 C 37.0 C; [redacted]20[redacted] (RX DAY 13): TEMPERATURE MEASUREMENTS: 38.0 C 37.1 C; [redacted]20[redacted] (RX DAY 14): TEMPERATURE MEASUREMENTS: 35.0 C

AE Stopped Rx Day	14
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	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:25
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はスイスの 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，出血性膀胱炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，TPMT（チオプリンメチルトランスフェラーゼ）のヘテロ接合性変異，元喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与12日後＊　　，被験者は出血性膀胱炎を発現した。投与14日後＊　　，出血性膀胱炎は消失した。

被験者は恥骨下に痛みがあり，腎臓に痛みはなかった。被験者に発熱はなく，心肺機能も安定していた。投与12日後＊　　，被験者は入院した。入院中，尿検査，CRP 検査，血液学的検査及び心電図が実施され，被験者は膀胱洗浄及び抗生物質の経口投与を受けた。投与13日後＊　，

膀胱洗浄用のカテーテルが抜去された。投与14日後＊　，被験者は症状が消失し，退院した。

投与された薬剤は，bactrim forte，novalgin，ciproxin，ringerfundin 及びクレキサンであった。

Causality for ABT-494 (Blinded)

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1)　Hemorrhagic cystitis (10019598)　(Cystitis haemorrhagic (10011793))　[v.21.0]　[10019598]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of HEMORRHAGIC CYSTITIS

- Investigator: Not Applicable

- AbbVie: Not Applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 130 U/L (normal 42 to 98)

[redacted] **20[redacted] CHOLESTEROL:** 5.5 MMOL/L (normal <5)

[redacted] **20[redacted] ECG:** Normal

[redacted] **20[redacted] GGT:** 110 U/L (normal <35)

[redacted] **20[redacted] HAEMOGLOBIN:** 117 G/L (normal 120 to 160)

[redacted] **20[redacted] HAEMOGLOBIN:** 118 G/L (normal 120 to 160)

[redacted] **20[redacted] HEMATOCRIT:** 0.364 no unit (normal 0.37 to 0.47)

[redacted] **20[redacted] HEMATOCRIT:** 0.355 no unit (normal 0.37 to 0.47)

[redacted] **20[redacted] PLATELET COUNT:** 417 G/L (normal 150 to 300)

[redacted] **20[redacted] PLATELET COUNT:** 387 G/L (normal 150 to 300)

[redacted] **20[redacted] URINE CULTURE:** Positive e-coli

[redacted] **20[redacted] URINE HEMOGLOBIN:** +++

[redacted] **20[redacted] URINE PH:** 6.0 no unit

[redacted] **20[redacted] URINE PROTEIN:** ++

[redacted] **20[redacted] URINE SPECIFIC GRAVITY:** 1.015 kg/L

[redacted] **20[redacted] WHITE BLOOD CELLS:** 13.3 G/L (normal 4 to 10)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 10.3 G/L (normal 4 to 10)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg	6[redacted]	MALE	WHITE

Medical History	Onset Year
DIABETES MELLITUS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HYPERTENSION	20[redacted]
OTHER: ARTHRITIS	19[redacted]
OTHER: FISTULA	20[redacted]
OTHER: HAY FEVER	19[redacted]
SLEEP APNEA	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SURGERY: KNEE REPLACEMENT RIGHT SIDE	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1.5 PACK	25	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 15 mg	15	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 47	47

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
CALCIUM CARBONATE;COLECALCIFEROL	500.000 mg	BID	Y-M: 20[redacted]
CICLOSPORIN	100 mg	BID	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
INVESTIGATIONAL DRUG	0.000 mg	OTHER: WEEKLY	Y-M: 20[redacted] / -296
TACROLIMUS	6 mg	BID	Y-M: 20[redacted] / -217
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -186
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -72
DALTEPARIN	5000 IU	QD	Y-M: 20[redacted] / -7
PROPOFOL	320 mg	PRN	Y-M: 20[redacted] / -7
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 OTHER: SACHET	BID	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -72	Y-M: 20[redacted] / 62
DALTEPARIN	5000 IU	QD	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / 36
RED BLOOD CELLS	2 IU	OTHER: ONLY 2 UNITS ON ONE DAY	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 47
PROPOFOL	150 mg	PRN	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 48
CALCIUM CARBONATE;COLECALCIFEROL	500/800 mg	QD	Y-M: 20[redacted] / 51	ONGOING
IRON	50 mg	QD	Y-M: 20[redacted] / 51	ONGOING
MAGNESIUM	5 mmol	BID	Y-M: 20[redacted] / 51	ONGOING
METAMIZOLE	500 mg	PRN	Y-M: 20[redacted] / 51	ONGOING
METOCLOPRAMIDE	4 mg	PRN	Y-M: 20[redacted] / 53	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 53	ONGOING

DEXAMETHASONE;TOBRAMYCIN	1/3 g	OTHER: 3-4 TIMES DAILY	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 61
CARBOMER	10 g	OTHER: HOURLY	Y-M: 20[redacted] / 61	ONGOING
MESALAZINE	1 g	QD	Y-M: 20[redacted] / 61	ONGOING
METFORMIN	500 mg	QD	Y-M: 20[redacted] / 61	ONGOING
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 62	ONGOING

Event #1: Event of Interest - Anemia

Event Description	ANAEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 36
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 47
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 48): CT ABDOMEN PELVIS: MODERATE WALL THICKENING OF THE WOLE COLON WITH REDUCED HAUSTRATION, MUSOSAL ENHANCEMENT AND INTESTINAL VASCULAR INJECTIONS; GASTROSCOPY: NO ABNORMAILTY DETECTED; [redacted]20[redacted] (RX DAY 53): SUBTOTAL COLECTOMY: PENDING

AE Stopped Rx Day	62 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	16 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	WORSENNING OF DISEASE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はスイスの 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，関節炎，潰瘍性大腸炎（全大腸炎型）の悪化，及び中等症から重症の活動性潰瘍性大腸炎であった。

Event 2 の臨床経過：

投与47日後＊，被験者は潰瘍性大腸炎の悪化を発現した。投与62日後＊，潰瘍性大腸炎の悪化は消失した。

投与47日後＊　　，被験者は潰瘍性大腸炎の悪化に対する予定された手術のために入院した（被験者は疾患の悪化の徴候及び症状を有していた）。投与48日後＊　，胃内視鏡検査では異常は認められなかった。投与53日後＊　，結腸亜全摘術を受けた。被験者には 3 単位の輸血が行われた。投与62日後＊　　，被験者は退院した。

投与された薬剤は，tobradex，lacrinorm，メトホルミン，pantozol，paspertin，calcimagon d3，magnesio card gran，maltofer，novalgin，salofalk，prednison 及び血液であった。

The patient's past medications include:

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

CALCIMAGON D3 for BONES ([redacted])

SANDIMMUN for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

GS-5745 for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

PREDNISOLON for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.0] [10009901]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: Worsening of disease.

- AbbVie: Event is clearly consistent with progression or worsening of the underlying disease, and is considered expected for this study.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] COLONOSCOPY:** Demarcation from the anal verge: 70; Central Reader Endoscopy Subscore: 3

[redacted] **20[redacted] CT ABDOMEN PELVIS:** moderate wall thickening of the whole colon with reduced haustration, musosal enhancement and intestinal vascular injections

[redacted] **20[redacted] GASTROSCOPY:** No abnormality detected

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: NO ADDITIONAL INFORMATION IS AVAILABLE	20[redacted]
DEPRESSION: NO OTHER INFORMATION IS AVAILABLE	20[redacted]
EYE DISEASE/DISORDER: MYOPIA	19[redacted]
HYPERLIPIDEMIA: NO ADDITIONAL INFORMATION AVAILABLE	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: C-DIFFICILE INFECTION	20[redacted]
OTHER: HYPERGLYCEMIA	20[redacted]
OTHER: HYPOALBUMINEMIA	20[redacted]
OTHER: INTERMITTENT HEADACHES	20[redacted]
OTHER: LOW THYROID STIMULATING HORMONE LEVEL	20[redacted]
OTHER: MICROSCOPIC HEMATURIA	20[redacted]
OTHER: RIGHT HAND PAIN	20[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
OTHER: STEROID INDUCED INSOMNIA	20[redacted]
OTHER: VITAMIN B12 DEFICIENCY	20[redacted]
OTHER: VITAMIN D DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SURGERY: ADENOIDECTOMY	19[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]
SURGERY: TONSILECTOMY	19[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 30 mg	30	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 13	13

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
PREDNISONE	60 mg	QD	Y-M: 20[redacted]
DROSPIRENONE;ETHINYLESTRADIOL	1 OTHER: TABLET	QD	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -342
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -319
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted] / -319
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -258
COLECALCIFEROL	1000 OTHER: UNITS	BID	Y-M: 20[redacted] / -140
PREDNISONE	60 mg	QD	Y-M: 20[redacted] / -152
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -153
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / -160
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / -166
CETIRIZINE	10 mg	PRN	Y-M: 20[redacted] / -138
VITAMIN B12 NOS	1000 ug	QD	Y-M: 20[redacted] / -101
IRON	18 mg	BID	Y-M: 20[redacted] / -107
MELATONIN	3 mg	PRN	Y-M: 20[redacted] / -69
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -69
RIZATRIPTAN	10 mg	PRN	Y-M: 20[redacted] / -23
SACCHAROMYCES BOULARDII	250 mg	BID	Y-M: 20[redacted] / -24
FENTANYL	50 ug	OTHER: ONCE	Y-M: 20[redacted] / -6

PROPOFOL	450 mg	OTHER: ONCE	Y-M: 20[redacted] / -6
MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE	1 OTHER: BOTTLE	OTHER: ONCE	Y-M: 20[redacted] / -7
LOPERAMIDE	2.000 mg	PRN	Y: 20[redacted]
MESALAZINE	2.4 g	BID	Y: 20[redacted]
MESALAZINE	4 g	QD	Y: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y: 20[redacted]
FLUOXETINE	20 mg	QD	Y: 20[redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y: 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
DROSPIRENONE;ETHINYLESTRADIOL	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	1000 OTHER: UNITS	BID	Y-M: 20[redacted] / -140	ONGOING
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / -166	ONGOING
CETIRIZINE	10 mg	PRN	Y-M: 20[redacted] / -138	ONGOING
VITAMIN B12 NOS	1000 ug	QD	Y-M: 20[redacted] / -101	ONGOING
IRON	18 mg	BID	Y-M: 20[redacted] / -107	ONGOING
MELATONIN	3 mg	PRN	Y-M: 20[redacted] / -69	ONGOING
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -69	Y-M: 20[redacted] / 13
RIZATRIPTAN	10 mg	PRN	Y-M: 20[redacted] / -23	ONGOING
SACCHAROMYCES BOULARDII	250 mg	BID	Y-M: 20[redacted] / -24	ONGOING
FENTANYL	50 ug	OTHER: ONCE	Y-M: 20[redacted] / -6	Y-M: 20[redacted] / -6
PROPOFOL	450 mg	OTHER: ONCE	Y-M: 20[redacted] / -6	Y-M: 20[redacted] / -6
MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE	1 OTHER: BOTTLE	OTHER: ONCE	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -6
GLUCOSE;SODIUM CHLORIDE	100 OTHER: ML/HOUR	OTHER: ONCE	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 13
METHYLPREDNISOLONE	20 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 15
HEPARIN	5000 OTHER: UNITS	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 16
HYDROCORTISONE	100 mg	BID	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15

LIDOCAINE	60 mg	OTHER: ONCE	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
PREDNISONE	15 mg	OTHER: ONCE	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
PROPOFOL	230 mg	OTHER: ONCE	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
SODIUM CHLORIDE	250 mL	OTHER: ONCE	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
HYDROCORTISONE	80 mg	BID	Y-M: 20[redacted] / 16	ONGOING
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 16	ONGOING
AZATHIOPRINE	100 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / -17
FLUOXETINE	20 mg	QD	Y: 20[redacted]	ONGOING
VITAMINS NOS	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING

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

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 13
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 13): STOOL NPTST081-C. DIFFICILE GDH ANTIGEN: NEGATIVE; STOOL NPTST082-C. DIFFICILE RAPID TOXIN: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 13): ABDOMINAL X-RAY: NO EVIDENCE OF INTRAPERITONEAL OR STERNODIAPHRAGMATIC AIR. NO EVIDENCE OF TOXIC MEGACOLON. THERE IS GAS WITHIN NONDILATED BOWEL LOOPS. THERE IS A NONOBSTRUCTIVE BOWEL GAS PATTERN.; [redacted]20[redacted] (RX DAY 15): FLEXIBLE SIGMOIDOSCOPY WITH BIOPSY: MILD DISTAL COLITIS INVOLVING DESCENDING AND SIGMOID COLON. MODERATE PROCTITIS.

AE Stopped Rx Day	16 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	KNOWN HISTORY OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event	
Event Description	REFRACTORY ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 40 (27 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 40): LAPAROSCOPIC PROCTOCOLECTOMY: SUCCESSFUL LAPAROSCOPIC PROCTOCOLECTOMY WITH CREATION OF DIVERTING LOOP ILEOSTOMY	
AE Stopped Rx Day	45 (32 DAYS AFTER LAST TREATMENT)
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ONGOING KNOWN HISTORY OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），クロストリジウム・ディフィシレ感染及び貧血であった。

Event 1 の臨床経過：

投与13日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与16日後＊　，潰瘍性大腸炎の悪化は消失した。

投与13日後＊　　，被験者は排便の回数の増加（1 日 10–12 回）及び血性下痢の増加があり，救急治療室を受診した。バイタルサイン及び腹部 X 線検査に異常は認められなかった。腹部 X 線検査では，合併症は認められなかった。被験者は入院し，ステロイドの静脈内投与及び経直腸投与を受けた。生検を伴う軟性 S 状結腸鏡検査が行われ，異形成を伴わない直腸の広範囲の潰瘍形成を伴う重症の活動性大腸炎が確認された。被験者の症状は改善し，安定状態で退院した。投与16日後＊　に退院し，自宅にて prednisone 40 mg を 1 日 1 回服用し，ヒドロコルチゾン注腸を 1 日 2 回行った。

投与された薬剤は，prednisone，ヘパリン，cortenema，cortifoam，ソル・メドロール及び dextrose・塩化ナトリウム合剤であった。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS (20[redacted])

LOPERAMIDE for ULCERATIVE COLITIS (20[redacted])

MESALAMINE for ULCERATIVE COLITIS (20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS (20[redacted])

SOLUMEDROL for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

BUDESONIDE for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Known history of ulcerative colitis.

- AbbVie: Recurring flare of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL X-RAY:** No evidence of intraperitoneal or sternodiaphragmatic air. No evidence of toxic megacolon. There is gas within nondilated bowel loops. There is a nonobstructive bowel gas pattern.

[redacted] **SIGMOIDOSCOPY:** Flexible sigmoidoscopy with biopsy: Mild distal colitis involving descending and sigmoid colon. Moderate proctitis.

[redacted] **STOOL CULTURE:** C. Difficile GDH antigen: negative

[redacted] **STOOL CULTURE:** C. Difficile rapid toxin: negative
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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，難治性の潰瘍性大腸炎の事象を発現した。関連する病歴は，潰瘍性大腸炎であった。

Event 2 の臨床経過：

投与40日後＊　，被験者は難治性の潰瘍性大腸炎を発現した。投与45日後＊　，難治性の潰瘍性大腸炎は消失した。

投与40日後＊　，被験者は入院した。入院歴及び身体検査により，被験者は難治性の潰瘍性大腸炎のための腹腔鏡下の直腸結腸切除術が計画され，この手術のために入院した。この重篤

な有害事象に関連する徴候及び症状は，下痢及び直腸出血であった。投与40日後＊　　，腹腔鏡下の直腸結腸切除術は成功し，便流変更性及びループ式の回腸瘻造設が行われた。入院中の術後の経過に問題はなかった。診断的検査及び臨床的に関連のある臨床検査の実施の有無は不明であった。投与45日後＊　　，被験者は退院した。

治験責任医師によると，本事象に関連のある被験者の危険因子は，最近の出来事として，潰瘍性大腸炎の悪化をステロイドで治療したことであった。本事象に関連のある家族歴は認められなかった。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS (20[redacted])

LOPERAMIDE for ULCERATIVE COLITIS (20[redacted])

MESALAMINE for ULCERATIVE COLITIS (20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS (20[redacted])

SOLUMEDROL for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

BUDESONIDE for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

SOLUMEDROL for WORSENING ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Blinded)

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1)　Ulcerative colitis (10045365)　(Colitis ulcerative (10009900))　[v.20.0]　[10045365]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of REFRACTORY ULCERATIVE COLITIS

- Investigator: Ongoing known history of ulcerative colitis.

- AbbVie: Recurring flare of pre-existing Ulcerative colitis

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
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg	2[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ENTAMOEBA HISTOLYTICA	20[redacted]
OTHER: HEMORRHOIDS	20[redacted]
OTHER: OCCASIONAL NIGHT SWEATS	20[redacted]
OTHER: RECTAL BLEEDING	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SURGERY: LEFT HAND SURGERY	20[redacted]
SURGERY: RIGHT INGUINAL HERNIA REPAIR	20[redacted]
SURGERY: RIGHT SHOULDER ARTHROSCOPY WITH LABRAL REPAIR	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 30 mg	30	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted]-[redacted] / -19
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -45
MAGNESIUM SULFATE;POTASSIUM SULFATE;SODIUM SULFATE	6 OTHER: OUNCES	OTHER: TWICE	Y-M: 20[redacted]-[redacted] / -10
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -14
PROPOFOL	300 mg	OTHER: DIVIDED DOSES	Y-M: 20[redacted]-[redacted] / -9
METRONIDAZOLE	NOT REPORTED	OTHER: UNKNOWN	Y: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y: 20[redacted]
OMEPRAZOLE	40 mg	QD	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -14	Y-M: 20[redacted]-[redacted] / 42
PREDNISONE	40 mg	QD	Y-M: 20[redacted]-[redacted] / 43	Y-M: 20[redacted]-[redacted] / 47
HYDROCORTISONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]-[redacted] / 45	Y-M: 20[redacted]-[redacted] / 47
METHYLPREDNISOLONE	60 mg	BID	Y-M: 20[redacted]-[redacted] / 48	Y-M: 20[redacted]-[redacted] / 53
PREDNISONE	40 mg	QD	Y-M: 20[redacted]-[redacted] / 54	ONGOING
OMEPRAZOLE	40 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 48 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 48): CT ABDOMEN AND PELVIS WITH IV CONTRAST ONLY: ABNORMAL THICKENING, MUCOSAL ENHANCEMENT, AND SURROUNDING INFLAMMATION OF THE DESCENDING COLON, SIGMOID COLON, AND RECTUM COMPATIBLE WITH STATED HISTORY OF ULCERATIVE COLITIS

AE Stopped Rx Day	54 (11 DAYS AFTER LAST TREATMENT)
Duration of AE	7 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HISTORY OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 2[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，潰瘍性大腸炎の再燃の事象を発現した。関連する病歴は，直腸出血，アメーバ赤痢，痔核，胃食道逆流性疾患，鉄欠乏性貧血，潰瘍性大腸炎（左側），手術（右鼡径部ヘルニア修復），現喫煙者（噛みタバコ）及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与48日後＊　　，被験者は潰瘍性大腸炎の再燃を発現した。投与54日後＊　，潰瘍性大腸炎の再燃は消失した。

本事象発現前の 投与43日後＊　　に，被験者は本治験を早期に中止するために来院した。

投与48日後＊，被験者は入院した。入院時，被験者には 1 日 20 回までの緊急及び頻回な排便，並びに複数回の夜間の下痢が見られた。血塊を伴う直腸出血が見られた。軽度の右腹部痛及び全般的な腹痛があった。被験者はステロイドの静脈内投与を受けた。被験者は症状の消失が遅く，入院が延長された。被験者は prednisone の経口投与を開始した。投与54日後＊，被験者は退院した。

投与された薬剤は，prednisone 及びソル・メドロールであった。

The patient's past medications include:

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

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

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

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

Causality for ABT-494 (Blinded)

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

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of ULCERATIVE COLITIS FLARE

- Investigator: The patient's history of ulcerative colitis.

- AbbVie: Recurring flare of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

Unknown date CLOSTRIDIUM DIFFICILE: negative for clostridium difficile and enteric pathogens.

[redacted] **20[redacted] COLONOSCOPY:** Left sided UC

[redacted] **20[redacted] COLONOSCOPY:** A clear demarcation between normal and inflamed colonic mucosa was seen at 30 cm (distance from the anal verge), Endoscopy subscore: 3

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** Impression: Abnormal thickening, mucosal enhancement, and surrounding inflammation of the descending colon, sigmoid colon, and rectum compatible with ulcerative colitis history

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: SUBJECT IS CURRENTLY TAKING IRON SUPPLEMENTS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: ACID REFLUX	20[redacted]
HYPERTENSION	20[redacted]
OTHER: ANXIETY	20[redacted]
OTHER: DX'D WITH CERVICAL CANCER AND SUCCESSFULLY TREATED AT THE AGE OF 25.	19[redacted]
OTHER: HEMORRHOIDS	20[redacted]
OTHER: JOINT PAIN	20[redacted]
OTHER: RIGHT SIDE FLANK PAIN	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo		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
ALPRAZOLAM	0.5 mg	OTHER: AT BEDTIME	Y-M: 20[redacted]-[redacted]
IRON	325 mg	QD	Y-M: 20[redacted]-[redacted]
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted]-[redacted]
QUETIAPINE	25 mg	OTHER: AT BEDTIME	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
MESALAZINE	3200 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	80 mg	QD	Y-M: 20[redacted]-[redacted]
HYDROCODONE;PARACETAMOL	7.5-325 mg	PRN	Y-M: 20[redacted]-[redacted] / -96
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]-[redacted] / -51
BIFIDOBACTERIUM BIFIDUM;LACTOBACILLUS ACIDOPHILUS	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted] / -65
VITAMINS NOS	UNKNOWN mg	QD	Y: 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
ALPRAZOLAM	0.5 mg	OTHER: AT BEDTIME	Y-M: 20[redacted]-[redacted]	ONGOING
IRON	325 mg	QD	Y-M: 20[redacted]-[redacted]	Y-M: 20[redacted]-[redacted] / 55
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted]-[redacted]	Y-M: 20[redacted]-[redacted] / 12
QUETIAPINE	25 mg	OTHER: AT BEDTIME	Y-M: 20[redacted]-[redacted]	ONGOING
HYDROCODONE;PARACETAMOL	7.5-325 mg	PRN	Y-M: 20[redacted]-[redacted] / -96	ONGOING
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]-[redacted] / -51	Y-M: 20[redacted]-[redacted] / 27
BIFIDOBACTERIUM BIFIDUM;LACTOBACILLUS ACIDOPHILUS	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted] / -65	Y-M: 20[redacted]-[redacted] / 39
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]-[redacted] / 12	ONGOING
CEFAZOLIN	1 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted]-[redacted] / 19	Y-M: 20[redacted]-[redacted] / 21

DOCOSANOL	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
VALACICLOVIR	1000 mg	BID	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 28
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 21
CEFALEXIN	500 mg	QID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 30
VITAMINS NOS	UNKNOWN mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 55

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

Event Description	FACIAL CELLULITIS
Preferred term	蜂巣炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 19
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	28
Duration of AE	10 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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，顔面の蜂巣炎の事象を発現した。関連する病歴は，潰瘍性大腸炎であった。

Event 1 の臨床経過：

投与19日後＊　，被験者は顔面の蜂巣炎を発現した。投与28日後＊　，顔面の蜂巣炎は消失した。

投与19日後＊　，被験者は口の左側の痛みから始まった顔面の蜂巣炎があり，入院した。顔面の蜂巣炎の徴候及び症状は，顔面左側の圧迫感及び疼痛，並びに耳及び首へ継続的に拡大する紅斑であった。投与21日後＊　，被験者は退院した。

投与された薬剤は，セファゾリン，abreva cream，ケフレックス，lovenox 及びバラシクロビルであった。

Causality for ABT-494 (Blinded)

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1)　Cellulitis of face (10007909)　(Cellulitis (10007882))　[v.21.0]　[10007909]

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 ABT-494 (Blinded)

Event of FACIAL CELLULITIS

- Investigator: Not applicable

- AbbVie: Not applicable

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ABT-494 45 mg	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	19[redacted]
NEPHROLITHIASIS	19[redacted]
OSTEOPOROSIS	20[redacted]
OTHER: BENZO ADDICTION	20[redacted]
OTHER: BIPOLAR DISORDER	20[redacted]
OTHER: BOWEL OBSTRUCTION	20[redacted]
OTHER: ENDOMETRIOSIS	19[redacted]
OTHER: FIBROMYALGIA	20[redacted]
OTHER: IRRITABLE BOWEL SYNDROME	19[redacted]
OTHER: RECURRENT UTIS	20[redacted]
OTHER: SCREENING PHYSICAL EXAM: DIFFUSE POSTERIOR THORAX AND BACK TENDERNESS	20[redacted]
OTHER: SCREENING PHYSICAL EXAM: MODERATE DIFFUSE ABDOMINAL TENDERNESS. NO MASSES. NO REBOUND	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SURGERY: APPENDECTOMY	20[redacted]
SURGERY: C-SECTION	19[redacted]
SURGERY: C-SECTION	19[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]
SURGERY: HERNIA REPAIR	20[redacted]
SURGERY: HYSTERECTOMY	20[redacted]

SURGERY: LEFT ANKLE SURGERY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	1	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	CURRENT	10 SESSIONS	1	
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
GABAPENTIN	600 mg	TID	Y-M: 20[redacted]-[redacted] / -102
PROMETHAZINE	25 mg	PRN	Y-M: 20[redacted]-[redacted] / -102
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]-[redacted] / -77
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted]-[redacted] / -77
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -77
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted]-[redacted] / -81
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]-[redacted] / -81
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted]-[redacted] / -82
SULFASALAZINE	1000 mg	TID	Y-M: 20[redacted]-[redacted] / -82
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -14
PREDNISONE	60 mg	OTHER: ONCE ONLY	Y-M: 20[redacted]-[redacted] / -15
CIPROFLOXACIN	500 mg	QD	Y-M: 20[redacted]-[redacted] / -32
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]-[redacted] / -10

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
GABAPENTIN	600 mg	TID	Y-M: 20[redacted] / -102	ONGOING
PROMETHAZINE	25 mg	PRN	Y-M: 20[redacted] / -102	ONGOING
SULFASALAZINE	1000 mg	TID	Y-M: 20[redacted] / -82	ONGOING
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 102
ACETYLSALICYLIC ACID;CAFFEINE	1 OTHER: PACKET	PRN	Y-M: 20[redacted] / 4	Y-M: 20[redacted] / 226
CIPROFLOXACIN	400 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
PIPERACILLIN;TAZOBACTAM	4.5 g	OTHER: ONCE ONLY	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
SODIUM CHLORIDE	2,409 mL	OTHER: ONCE ONLY	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 30
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 36
PARACETAMOL	325 mg	PRN	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 47

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

Event Description	SEPSIS, RSV RESPIRATORY INFECTION
Preferred term	RS ウイルス感染，敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 28
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 28): Creatinine: 233.384606 [44.20163 - 132.60489] UMOL/L; Leukocytes: 20.3 [3.8 - 12.8] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 28): CT HEAD WO CONTRAST: NO DEFINITE ACUTE INTRACRANIAL ABNORMALITY.; XR CHEST: THE HEART DOES NOT APPEAR SIGNIFICANTLY ENLARGED. THERE ARE LOW LUNG VOLUMES. THERE IS MILD INFILTRATE IN THE LEFT MID LUNG AND POTENTIAL VERY MILD MEDIAL RIGHT BASILAR INFILTRATE.

AE Stopped Rx Day	31
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO

SAE Criteria HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:25
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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，敗血症及び RS ウイルス呼吸器感染症の事象を発現した。関連する病歴は，ベンゾジアゼピン依存症，高血圧，反復性尿路感染症及び潰瘍性大腸炎であった。

Event 1 の臨床経過：

投与28日後＊　，被験者は敗血症及び RS ウイルス呼吸器感染症を発現した。　投与31日後＊，敗血症及び RS ウイルス呼吸器感染症は消失した。

投与28日後＊　，被験者は意識障害を呈し，自分の近況を思い出せない状態で救急治療室を受診した。胸部X線検査及び頭部 CT スキャン検査が行われ，入院前に救急科で輸液，ゾシン及び cipro を投与された。腰椎穿刺が試みられたが，被験者の体質のために成功しなかった。被験者は，輸液の投与及び抗生物質の経験的治療を開始し，その後症状は改善した。　投与31日後＊，被験者は退院した。被験者は，退院時に治験薬の投与を再開した。

投与された薬剤は，塩化ナトリウム 0.9%，アセトアミノフェン，ゾシン，cipro 及びオキシコドンであった。

The patient's past medications include:

CIPRO for UTI ([redacted]20[redacted] - [redacted]20[redacted], [redacted]20[redacted] - [redacted]20[redacted])

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

Causality for ABT-494 (Blinded)

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1) Sepsis (10040047) (Sepsis (10040047)) [v.20.0] [10040047]

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

2) Respiratory syncytial virus infection (10061603) (Respiratory syncytial virus infection (10061603)) [v.20.0] [10061603]

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 ABT-494 (Blinded)

Event of SEPSIS

- Investigator: N/A

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** Low lung volumes and mild infiltrate in left mid lung and potential very mild medial right basilar infiltrate.

[redacted] **20[redacted] CREATININE:** 2.64 mg/dL (normal 0.5 to 1.5)

[redacted] **20[redacted] HEAD CT:** Mild motion artifact but no acute intracranial abnormali

[redacted] **20[redacted] WBC:** 20.3 K/UL (normal 3.8 to 12.8)

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
結腸異形成	X	X		
鉄欠乏性貧血				X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 45 mg	5[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: INTERMITTENT FEVER, RELATED TO STUDY CONDITION	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	More than 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISONE	35 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -333
LOPERAMIDE	UNK mg	PRN	Y-M: 20[redacted] / -214
DICYCLOVERINE	20 mg	BID	Y-M: 20[redacted] / -49
MESALAZINE	4.8 g	QD	Y: 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
LOPERAMIDE	UNK mg	PRN	Y-M: 20[redacted] / -214	ONGOING
DICYCLOVERINE	20 mg	BID	Y-M: 20[redacted] / -49	ONGOING
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 27
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 31
IRON	300 mg	OTHER: 3 TIMES	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 45
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 39
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 46
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 53
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 61
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 69
ENOXAPARIN	90 mg	BID	Y-M: 20[redacted] / 92	ONGOING

Event #1: Event of Interest - Anemia

Event Description IRON DEFICIENCY ANEMIA

Preferred term 鉄欠乏性貧血

AE Onset Date / Rx Day [redacted]20[redacted] / 15

Age at AE Onset 5[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Rx Day 45

Duration of AE	31 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	HIGH GRADE DYSPLASIA IN LEFT COLON
Preferred term	結腸異形成
AE Onset Date / Rx Day	[redacted]20[redacted] / 57
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 57): NPTST474-SURGICAL PATHOLOGY: FOCAL HIGH GRADE DYS [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 57): BIOPSY, COLON: LEFT COLON, FOCAL HIGH GRADE DYSPLASIA; [redacted]20[redacted] (RX DAY 93): COLECTOMY: DISCHARGED [redacted]/[redacted]/20[redacted]

AE Stopped Rx Day	93 (36 DAYS AFTER LAST TREATMENT)
Duration of AE	37 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左結腸の高度異形成の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 4 杯以上）であった。

Event 2 の臨床経過：

投与57日後＊　，被験者は左結腸の高度異形成を発現した。投与93日後＊　，左結腸の高度異形成は消失した。

本事象の発現前に，被験者は潰瘍性大腸炎の症状が悪化していた。投与57日後＊　，結腸内視鏡検査における病理組織学的検査で，高度異形成が認められた。治験薬の投与は完全に中止され，結腸切除術が計画された。投与86日後＊　，結腸切除術前の画像診断で両側の肺塞栓が認められ，被験者は回収型下大静脈フィルターを留置された。投与92日後＊　，被験者は高度異形成のための腹腔内結腸切除術を受けるため，入院した。投与93日後＊　，被験者は腹腔内結腸全摘術を受けた。結腸切除術の病理組織学的検査では，潰瘍性大腸炎に対応する活動期の慢性大腸炎の所見が著しく見られた。組織は，軽度異形成及び局所的には高度異形成を示していた。癌の徴候は認められなかった。組織の断端では，異形成は見られなかった。また，虫垂では線維性の閉塞が見られた。被験者は 投与98日後＊　に退院した。

診療記録によると，被験者は結腸切除術によく耐え，術後の経過に問題はなかった。痛みは自己調節鎮痛法での麻酔薬でコントロールされ，その後，経口の鎮痛剤に移行した。また，電解質の状態を注意深く観察し，必要に応じて水分を補給した。腸の機能が回復したため経口食を開始し，摂取できた。ストーマの管理を行う看護師と協力してストーマの管理を行った。退院時，被験者は悪心や嘔吐もなく経口食を摂取し，痛みは経口の鎮痛剤で十分に管理され，予想通りに歩行及び排泄が可能であった。

The patient's past medications include:

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

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

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

VENOFER for ULCERATIVE COLITIS / IRON DEFICIENCY ANEMIA and ULCERATIVE COLITIS / IRON DEFICIENCY ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

MESALAMINE for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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1) Colon dysplasia (10071161) (Colon dysplasia (10071161)) [v.21.0] [10071161]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of HIGH GRADE DYSPLASIA IN LEFT COLON

- Investigator: Not applicable

- AbbVie: Weak temporal association with close to 2 months of study drug exposure. Additional risk factors include pre-existing ulcerative colitis and alcohol consumption of more than 4 drinks per day.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BICARB:** 23 no units

[redacted] **20[redacted] BIOPSY, COLON:** Left colon, focal high grade dysplasia

[redacted] **20[redacted] BODY TEMPERATURE:** 98.5 degrees F

[redacted] **20[redacted] BUN:** 12 no units

[redacted] **20[redacted] CALCIUM:** 8.9 no units

[redacted] **20[redacted] CL:** 101 no units

[redacted] **20[redacted] COLONOSCOPY:** High grade dysplasia

[redacted] **20[redacted] CREATININE:** 0.99 no units

[redacted] **20[redacted] CT CHEST/ABDOMEN/PELVIS WITH CONTRAST:** CT colonic findings consistent with known ulcerative colitis and without evidence of mass, complications, or metastasis in abdomen or pelvis. Incidental near completely occlusive segmental acute pulmonary emboli bilaterally. No evidence of heart strain or pulmonary infarct.

[redacted] **20[redacted] HCT:** 35 no units

[redacted] **20[redacted] HGB:** 11.3 no units

[redacted] **20[redacted] K:** 3.9 no units

[redacted] **20[redacted] NA:** 140 no units

[redacted] **20[redacted] PLT:** 348 no units

[redacted] **20[redacted] WBC:** 10.8 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
腹痛	X			
発熱	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 45 mg	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: INTERMITENT	20[redacted]
DRUG ALLERGIES/REACTIONS: BODY ACHES FROM PREDNISONE	20[redacted]
LEFT SIDED UC	20[redacted]
MIGRAINE HEADACHE	20[redacted]
OTHER: ABDOMINAL BLOATING	20[redacted]
OTHER: ANXIETY SECONDARY TO PREDNISONE USE	20[redacted]
OTHER: CHRONIC DIARRHEA	20[redacted]
OTHER: ECZEMA	20[redacted]
OTHER: FEVER RESULTING FROM UC FLARES	20[redacted]
OTHER: HEMORRHOIDS	20[redacted]
OTHER: HUMAN PAPILLOMAVIRUS	20[redacted]
OTHER: INSOMNIA SECONDARY TO PREDNISONE USE	20[redacted]
OTHER: LOW BLOOD PRESSURE	20[redacted]
OTHER: LOWER BACK PAIN DUE TO MENSES	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

PIPES	NEVER

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45	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
CALCIUM CARBONATE	2 OTHER: TABLETS	PRN	Y-M: 20[redacted]
LOPERAMIDE	2 OTHER: TABLETS	PRN	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
MELATONIN	3 mg	PRN	Y-M: 20[redacted]
SIMETICONE	2 OTHER: TABLETS	PRN	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -304
AZATHIOPRINE	75 mg	QD	Y-M: 20[redacted] / -213
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -213
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -182
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -121
BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM BREVE;BIFIDOBACTERIUM INFANTIS;LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS DELBRUECKII;LACTOBACILLUS PARACASEI;LACTOBACILLUS PLANTARUM;STREPTOCOCCUS THERMOPHILUS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / -25
HAMAMELIS VIRGINIANA	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -29
PARACETAMOL	500 mg	QID	Y-M: 20[redacted] / -6
MESALAZINE	1.5 g	QD	Y: 20[redacted]
CALCIUM;VITAMIN D NOS	1300 mg	QD	Y: 20[redacted]
FISH OIL	1 OTHER: CAPSULE	QD	Y: 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 / Stop Year-Month / RX Day	
CALCIUM CARBONATE	2 OTHER: TABLETS	PRN	Y-M: 20[redacted]	ONGOING
LOPERAMIDE	2 OTHER: TABLETS	PRN	Y-M: 20[redacted]	ONGOING
MELATONIN	3 mg	PRN	Y-M: 20[redacted]	ONGOING
SIMETICONE	2 OTHER: TABLETS	PRN	Y-M: 20[redacted]	ONGOING
BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM BREVE;BIFIDOBACTERIUM INFANTIS;LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS DELBRUECKII;LACTOBACILLUS PARACASEI;LACTOBACILLUS PLANTARUM;STREPTOCOCCUS THERMOPHILUS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / -25	ONGOING
HAMAMELIS VIRGINIANA	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -29	ONGOING
PARACETAMOL	500 mg	QID	Y-M: 20[redacted] / -6	Y-M: 20[redacted] / -2
METHYLPREDNISOLONE	60 mg	OTHER: Q. 6 HRS THEN Q. 8 HRS	Y-M: 20[redacted] / 4	Y-M: 20[redacted] / 5
METHYLPREDNISOLONE	30 mg	OTHER: Q. 12 HOURS	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 7
CINCHOCAINE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 22
DICYCLOVERINE	20 mg	QID	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 22
LORAZEPAM	0.5 mg	OTHER: EVERY 8 HOURS AS NEEDED	Y-M: 20[redacted] / 7	ONGOING
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 29
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 30
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 7	ONGOING
TEMAZEPAM	15 mg	OTHER: QHS AS NEEDED	Y-M: 20[redacted] / 7	ONGOING
CALCIUM;VITAMIN D NOS	1300 mg	QD	Y: 20[redacted]	ONGOING
FISH OIL	1 OTHER: CAPSULE	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	ABDOMINAL PAIN, FEVER
Preferred term	腹痛，発熱
AE Onset Date / Rx Day	[redacted]20[redacted] / 3
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 4): Alanine Aminotransferase: 13 [5 - 30] U/L; Albumin: 24 [33 - 49] G/L; Alkaline Phosphatase: 98 [50 - 100] U/L; Aspartate Aminotransferase: 11 [5 - 30] U/L; Bicarbonate: 24 [17 - 30.6] MMOL/L; Blood Urea Nitrogen: 2.14182 [1.42788 - 8.56728] MMOL/L; Chloride: 99 [94 - 106] MMOL/L; Creatinine: 78.678901 [35.361304 - 97.243586] UMOL/L; Glucose: 4.884616 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.387 [0.34 - 0.48] FRACTION OF 1; Hemoglobin: 131 [116 - 164] G/L; Leukocytes: 13 [6.9 - 15] 10^9/L; NPTST487-TOTAL BILIRUBIN: 0.3 [0.2 - 1.2] MG/DL; Platelets: 448 [140 - 400] 10^9/L; Potassium: 3.5 [3.4 - 5.4] MMOL/L; Sodium: 132 [132 - 147] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 4): CT SCAN OF THE ABDOMEN AND PELVIS: EXTENSIVE INFLAMMATORY CHANGES OF THE COLON AND RECTUM WITH ULCERATIVE COLITIS WITH ACTIVE INFLAMMATORY DISEASE.; PHYSICAL EXAMINATION: VITAL SIGN TEMPERATURE AT T-MAX 38 CELSIUS: 36.5 CELSIUS AT RESOLUTION

AE Stopped Rx Day	25
Duration of AE	23 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FEVER ABOVE 39.0 CELSIUS AND ABDOMINAL PAIN SECONDARY TO ULERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:25

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，腹痛及び発熱の事象を発現した。

Event 1 の臨床経過：

投与3日後＊　，被験者は腹痛及び発熱を発現した。投与25日後＊　，腹痛及び発熱は消失した。

被験者は 2[redacted]歳女性で，投与5年前＊に潰瘍性大腸炎と診断された。最初に潰瘍性大腸炎と診断された時，被験者は結腸内視鏡検査を受け，汎大腸炎と判明した。被験者は apriso の服用を開始し，症状はすぐに改善した。被験者は継続して薬を服用する必要があることを理解しておらず，数ヶ月後に薬の服用を中止した。被験者は，他州へ引越しするまでは体調が良かったが，その後血性下痢を再発し，症状が悪化した。apriso を再開したが，効果が出るまでにより長い時間を要した。被験者は，短期間 apriso を続けた。血性下痢の症状が再発するまでは，被験者は薬の服用を再度中止していたと思われた。血性下痢の症状が再発した時，被験者はステロイドでの治療を受けた。被験者は，薬剤をエンタイビオに変更し，数ヶ月間服用したが改善せず，その後レミケードを開始した。レミケードでは症状が抑えられず，投与量を増やしたものの，症状は悪化し続けた。被験者は，現在ステロイドでの治療を受けており，他州への引越しを計画していた。被験者は，約 10 日前に結腸内視鏡検査を受けており，その報告書は持参していなかったが，重症の汎大腸炎と報告されたとのことであった。被験者は，今週の初めに本治験に参加し，盲検化された治験薬を数回服用した。先週から血性下痢を伴う腹痛が悪化し，1 日の排便回数が 10–15 回になった。また，被験者は微熱を訴え，それに伴う体重減少も認められた。治験薬は投与3日後＊　から休薬していた。投与4日後＊　，被験者は，発熱及び腹痛があり，入院した。被験者の体温は摂氏 38°C であった。被験者は絶食下で，ステロイドであるソル・メドロール 60 mg の 6 時間毎の静脈内投与を開始し，その後，まず投与間隔を 8 時間毎に変更し，次に投与量及び投与間隔を 30 mg 及び 12 時間毎に変更し，固形食の摂取に戻った。投与7日後＊，被験者は，prednisone 40 mg の 1 日 1 回経口投与により安定した状態で退院した。

投与された薬剤は，ソル・メドロール，prednisone，zofran，prilosec 及び bentyl であった。

The patient's past medications include:

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

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

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

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

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

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

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

Causality for ABT-494 (Blinded)

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1) Abdominal pain (10000081) (Abdominal pain (10000081)) [v.21.0] [10000081]

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

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

Dechallenge: No

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

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of ABDOMINAL PAIN, FEVER

- Investigator: FEVER ABOVE 39.0 CELSIUS AND ABDOMINAL PAIN SECONDARY TO ULERATIVE COLITIS.

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 13 U/L (normal 5 to 30)

[redacted] **20[redacted] ALBUMIN:** 2.4 G/DL (normal 3.3 to 4.9)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 98 U/L (normal 50 to 100)

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 11 U/L (normal 5 to 30)

[redacted] **20[redacted] BICARBONATE:** 24 MEQ/L (normal 17.0 to 30.6)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 6 mg/dL (normal 4 to 24)

[redacted] **20[redacted] BODY TEMPERATURE:** 38.0 Degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** 36.5 Degrees C

[redacted] **20[redacted] CHLORIDE:** 99 MMOL/L (normal 94 to 106)

[redacted] **20[redacted] COLONOSCOPY:** No normal mucosa (pancolitis)

[redacted] **20[redacted] CREATININE:** 0.89 mg/dL (normal 0.4 to 1.1)

[redacted] **20[redacted] CT SCAN OF ABDOMEN AND PELVIS:** Extensive inflammatory changes of the colon and rectum with ulcerative colitis, with active inflammatory disease.

[redacted] **20[redacted] GLUCOSE:** 88 mg/dL (normal 70 to 100)

[redacted] **20[redacted] HEMATOCRIT:** 38.7 % (normal 34 to 48)

[redacted] **20[redacted] HEMOGLOBIN:** 13.1 G/DL (normal 11.6 to 16.4)

[redacted] **20[redacted] PLATELET COUNT:** 448 X10**3/MCL (normal 140 to 400)

[redacted] **20[redacted] POTASSIUM:** 3.5 MEQ/L (normal 3.4 to 5.4)

[redacted] **20[redacted] SODIUM:** 132 MEQ/L (normal 132 to 147)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 0.3 mg/dL (normal 0.2 to 1.2)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 13.0 X10**3/MCL (normal 6.9 to 15.00)

M14-234 試験 Substudy 2

治験の標題： 中等症から重症の活動性潰瘍性大腸炎患者を対象としたウパダシチニブ（ABT-494）の導入療法及び維持療法における安全性及び有効性を評価する多施設共同無作為化二重盲検プラセボ対照試験
施設数 / 実施国名： 199 施設（アルゼンチン，オーストラリア，オーストリア，ベルギー，ボスニア・ヘルツェゴビナ，ブラジル，カナダ，中国，クロアチア，チェコ共和国，エストニア，フィンランド，フランス，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，ノルウェー，ポーランド，ポルトガル，ロシア，セルビア，スロバキア，南アフリカ，スペイン，スイス，台湾，トルコ，イギリス及び米国）
治験調整医師： [redacted], MD, PhD
公表文献（参考資料）： 14 報
治験期間： 最初の被験者の初回来院日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日 開発のフェーズ： 第 III 相
目的： 中等症から重症の活動性潰瘍性大腸炎（以下「UC」）患者のうち，アミノサリチル酸製剤，免疫調節薬，副腎皮質ステロイド又は生物学的製剤に対して効果不十分，効果減弱又は不耐容であった患者を対象として，寛解導入（Adapted Mayo スコアによる）におけるウパダシチニブ 45 mg 1 日 1 回投与の有効性及び安全性をプラセボと比較して評価する。
被験者数（計画時と解析時）： 計画時：462 例，解析時：474 例
診断と主要な組入れ基準： 主要な選択基準：ベースライン時の年齢が 16 歳以上 75 歳以下の男女で，ベースラインの 90 日以上前に UC と診断され，スクリーニング期間中に全大腸内視鏡検査で診断が確認されると共に，現在の感染症，上皮異形成及び/又は悪性腫瘍が除外されている患者。Adapted Mayo スコアが 5–9，かつ内視鏡サブスコアが 2–3（中央判定による評価）の活動性 UC を有しており，経口アミノサリチル酸製剤，副腎皮質ステロイド，免疫調節薬及び/又は生物学的製剤のいずれかひとつ以上に対して効果不十分，効果減弱又は不耐容である患者。健康状態にその他の問題がない患者。 主要な除外基準：クローン病と診断されている患者。劇症の大腸炎及び/又は中毒性巨大結腸症と診断されている患者。病変が直腸のみに限局している患者。結腸全摘術若しくは結腸亜全摘術，回腸瘻，Kock パウチ又は回腸ストマ造設の既往がある患者，又は腸管の手術を予定している患者。副腎皮質ステロイド，免疫調節薬等の治験実施計画書に規定された併用禁止薬を投与された患者。
治験方法： M14-234　　試験 Substudy（以下「SS2 は，中等症から重症の活動性 UC 患者を対象として，最長 16 週間の導入療法におけるウパダシチニブ 45 mg 経口投与の有効性及び安全性をプラセボと比較して評価する 2 つのパートで構成される第 III 相用量検証試験であった。8 週間の導入療法期である Part 1 では，被験者 474 例を 2：1 の比率で，二重盲検下でウパダシチニブ（319 例）又はプラセボ（155 例）のいずれかにランダム化した。ベースラインでの Bio-IR の状態（生物学的製剤に対して効果不十分，効果減弱又は不耐容［以下「Bio-IR」］，若しくは従来の治療に対して効果不十分，効果減弱又は不耐容を示すものの生物学的製剤は無効ではない［以下「Non-bio-IR」］），副腎皮質ステロイドの使用（あり又はなし）及び Adapted Mayo スコア（7 以下又は 7 超）を因子として層別化した。更に，Bio-IR については生物学的製剤の前治療歴（1 回以下又は 1 回超）， 1

Non-bio-IR については生物学的製剤の前治療歴（あり又はなし）により層別化した。Part 1 の投与 8 週時に Adapted Mayo スコアによる臨床的改善を達成しなかった被験者は Part 2 に移行した。Part 2 では，すべての被験者（144 例）にウパダシチニブ 45 mg を投与した（Part 1 でプラセボ投与：85 例，Part 1 でウパダシチニブ 45 mg 投与：59 例）。

被験薬，用量，投与方法及びロット番号：

被験薬	用量	投与方法	バルクロット番号
ウパダシチニブ	45 mg	経口	[redacted]

治療期間：

Part 1：8 週間，Part 2：8 週間

対照薬，用量，投与方法及びロット番号：

ウパダシチニブに対応するプラセボの経口フィルムコート錠 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 8 週時の Adapted Mayo スコアによる臨床的寛解率（Adapted Mayo スコアが 2 以下で，排便回数サブスコア［以下「SFS」］が 1 以下かつベースラインを超えない，直腸出血サブスコア［以下「RBS」］が 0，かつ内視鏡サブスコアが 1 以下）とした。ただし，M14-234　　試験 SS 2 では，内視鏡検査中に脆弱性を示す所見が認められ，その他の内視鏡的活動が「軽度」の場合，内視鏡サブスコアは 2 とした。

順位付き副次評価項目は，M14-234 試験 SS 1 と同じ定義を用いて，投与 8 週時又は投与 2 週時（部分的 Adapted Mayo スコアによる臨床的改善率のみ）に評価した。

1. 内視鏡的改善率（内視鏡サブスコアが 0 又は 1）
2. 内視鏡的寛解率（内視鏡サブスコアが 0）
3. Adapted Mayo スコアによる臨床的改善率（Adapted Mayo スコアのベースラインからの減少が 2 以上かつ 30%以上，更に RBS の減少が 1 以上又は RBS が 1 以下）
4. 部分的 Adapted Mayo スコアによる臨床的改善率（部分的 Adapted Mayo スコアのベースラインからの減少が 1 以上かつ 30%以上，更に RBS の減少が 1 以上又は RBS が 1 以下）
5. 組織学的－内視鏡的粘膜改善率（内視鏡サブスコアが 1 以下及び Geboes スコアが 3.1 以下）
6. 便意切迫感を報告しなかった被験者の割合
7. 腹痛を報告しなかった被験者の割合
8. 組織学的改善率（Geboes スコアがベースラインから減少）
9. Inflammatory bowel disease questionnaire（以下「IBDQ」）合計スコアのベースラインからの変化量
10. 粘膜治癒率（内視鏡サブスコアが 0 及び Geboes スコアが 2 未満）
11. Functional assessment of chronic illness therapy-fatigue（以下「FACIT-F」）スコアのベースラインからの変化量

薬物動態：

ウパダシチニブ 45 mg 1 日 1 回投与後のウパダシチニブの血漿中濃度の平均値（標準偏差）を，前回投与からの時間ごとに要約した。

安全性：

有害事象，バイタルサイン，身体検査，臨床検査値（血液学的検査，血液生化学検査及び尿検査）及び治験薬に係る苦情を評価した。

統計手法：

有効性：

主要評価項目は，投与 8 週時の Adapted Mayo スコアによる臨床的寛解率とした。主要な estimand は，intent to treat（以下「ITT」）集団を対象とした投与 8 週時の Adapted Mayo スコアによる臨床的寛解（治験薬の早期中止の有無は問わず，UC に関連する副腎皮質ステロイドの開始又は増量がない）を達成した被験者の割合に関するウパダシチニブ 45 mg 1 日 1 回群（以下「45 mg 群」）及びプラセボ 1 日 1 回群（以下「プラセボ群」）間の差とした。主要評価項目の解析では，欠測データを扱うための主要な解析手法としてノンレスポンダーインピュテーション（以下「NRI」）-C を用いた。NRI-C では，新型コロナウイルス感染症（以下「COVID-19」）又は COVID-19 感染拡大に関連する物流上の制限による欠測データは多重補完法を用い，それ以外の規定された来院の許容期間中に評価されなかった被験者（欠測又は試験の早期中止のいずれも）は非改善例として取り扱った。主要解析では，8 週間の二重盲検導入療法期である Part 1 でランダム化し，二重盲検下で治験薬を 1 回以上投与した被験者（以下「ITT1 集団」）を対象として 45 mg 群とプラセボ群間の臨床的寛解率を比較した。主要評価項目の投与群間差は，Bio-IR の状態（Bio-IR 又は Non-bio-IR），ベースラインでの副腎皮質ステロイドの使用（あり又はなし）及びベースラインでの Adapted Mayo スコア（7 以下又は 7 超）を層別因子とした Cochran Mantel Haenszel（以下「CMH」）検定を用いて評価した。臨床的寛解率の投与群間差について，CMH に基づいた両側 95%信頼区間を算出した。

主要評価項目の感度分析は，COVID-19 による欠測データを扱うための特別な解析手法を用いない NRI（NRI-NC），ハイブリッド多重補完法（HMI）及び as observed（以下「AO」）を用いて解析した。また，選択した逸脱が発生した被験者を除外した補足的な解析も実施した。

Part 1 の有効性の副次評価項目では ITT1 集団を対象とし，2 値変数の評価項目は CMH 検定により解析し，欠測データを扱うための主要な解析手法として NRI-C を用いた。感度分析は，NRI-NC を用いて解析した。連続変数の評価項目は，混合効果・反復測定モデル（MMRM）を用いて解析し，AO 及び Delta-Based Multiple Imputation（DBMI）（事後解析）を用いた解析も実施した。

薬物動態：

各来院時での被験者別のウパダシチニブの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。

安全性：

標準的な安全性解析として，有害事象，特に注目すべき有害事象，臨床検査値及びバイタルサインを評価した。安全性解析対象集団（Part 1 の被験者［SA1 集団］，Part 2 の被験者［SA2 集団］）を対象として，安全性についてウパダシチニブ群とプラセボ群間の比較を行った。安全性評価項目は，実際の投与に基づいた投与群ごとに要約した。有害事象については，投与群別に ICH 国際医薬用語集（MedDRA）version 23.0 を用いて発現被験者数及び発現割合を要約した。安全性評価項目の連続変数（臨床検査値及びバイタルサインのベースラインからの変化量等）の投与群間差は，投与群を項とする分散分析モデルを用いて評価した。

有効性の結果

投与 8 週時に評価するすべての評価項目及び投与 2 週時の部分的 Adapted Mayo スコアによる臨床的改善率について，プラセボ群と比較して 45 mg 群で統計学的に有意な改善が認められ（$P < 0.001$），主要評価項目である Adapted Mayo スコアによる臨床的寛解率及びすべての順位付き副次評価項目を達成した。これらの評価項目から，疾患活動性及び症状，内視鏡的及び組織学的評価，炎症のバイオマーカー並びに生活の質（以下「QOL」）などの様々な領域の改善について，プラセボ群と比較して 45 mg 群で高い有効性が示された。また，Part 1 でウパダシチニブ 45 mg を 8 週間投与し，臨床的改善を達成しなかった被験者では，Part 2 の投与 16 週時の Adapted Mayo スコアによる臨床的改善率は 50.8%（30/59 例）であった。これより，ウパダシチ

ニブ 45 mg 1 日 1 回投与による導入療法の投与 8 週時までに臨床的改善を達成しなかった被験者でも，投与 16 週時まで延長投与することにより，ベネフィットが得られる可能性が示された。

ウパダシチニブ 45 mg 1 日 1 回投与による 8 週間の導入療法を受けた被験者では，IBDQ，European Quality of Life-5 Dimensions 5 Levels（EQ-5D-5L），Work Productivity and Activity Impairment Questionnaire（WPAI），FACIT-F，Ulcerative Colitis Symptoms Questionnaire（UC-SQ）及び 36-item short-form health survey（SF-36）のベースラインからの変化量はプラセボ群と比較して 45 mg 群の方が大きく，QOL に関するすべての評価項目でもベースラインからの大きな改善が認められた。これらの改善は投与 2 週時と早期から認められた。

以上の結果から，ウパダシチニブ 45 mg 1 日 1 回投与は，中等症から重症の活動性 UC 患者を対象とした導入療法として有効であることが示された。

薬物動態の結果

ウパダシチニブの血漿中濃度の平均値は，ウパダシチニブ 45 mg 1 日 1 回投与後 24 時間以内で 14.6–82.1 ng/mL の範囲であった。ウパダシチニブの血漿中濃度は，過去にウパダシチニブの第 III 相試験で認められた薬物動態と一致していた。

安全性の結果

- Part 1 では，有害事象，治験薬と関連ありの有害事象及び重篤な有害事象の発現割合は，45 mg 群とプラセボ群で同程度であり，高度の有害事象及び治験薬の投与中止に至った有害事象の発現割合は 45 mg 群の方が低かった。死亡は認められなかった。特に注目すべき有害事象の好中球減少症及びクレアチンホスホキナーゼ増加の発現割合は，プラセボ群と比較して 45 mg 群の方が高かった。
- Part 1 では，発現割合が 5%以上であった有害事象は，45 mg 群では認められず，プラセボ群では潰瘍性大腸炎及び貧血であった。Part 1 で 45 mg 群で多く認められた（発現割合が 4%以上）有害事象は，ざ瘡，血中クレアチンホスホキナーゼ増加，上咽頭炎及び頭痛であった。
- Part 1 では，重篤な有害事象の発現割合はプラセボ群で 5.8%であり，45 mg 群で 5%未満であった。最も多く認められた重篤な有害事象は，潰瘍性大腸炎であった。
- M14-234 試験 SS 2（Part 1 及び Part 2）では，特に注目すべき有害事象のうち，活動性結核，悪性腫瘍，非黒色腫皮膚癌（以下「NMSC」）を除く悪性腫瘍，NMSC，リンパ腫，腎機能障害，消化管穿孔，主要心血管事象，その他の心血管事象及び血栓症は認められなかった。Part 1 では，クレアチンホスホキナーゼ増加の発現割合は，プラセボ群（1.9%，3 例）と比較して 45 mg 群（5.0%，16 例）の方が高かった。好中球減少症及びリンパ球減少症の発現割合も，プラセボ群（いずれも 0.6%）と比較して 45 mg 群（それぞれ 5.0%及び 3.1%）の方が高かったが，貧血の発現割合は，プラセボ群（9.0%）と比較して 45 mg 群（3.1%）の方が低かった。
- Part 1 では，投与 8 週時の血液学的検査のベースラインからの平均変化量（最小二乗平均）について，ヘモグロビン量，血小板数及び好中球数は，プラセボ群と比較し

て 45 mg 群で大きな減少が認められた。リンパ球数は，45 mg 群とプラセボ群で同程度の減少が認められた。

- Part 1 では，投与 8 週時の血液生化学検査のベースラインからの平均変化量について，アスパラギン酸アミノトランスフェラーゼ（AST），アラニンアミノトランスフェラーゼ（ALT），クレアチンキナーゼ，クレアチニン及びコレステロールは，プラセボ群と比較して 45 mg 群で増加が認められた。
- Part 1 では，Grade 3 のヘモグロビン量減少が認められた被験者の割合は，45 mg 群と比較してプラセボ群の方が高かった。Grade 3 以上のリンパ球数減少が認められた被験者の割合は，プラセボ群と比較して 45 mg 群の方が高かった。Grade 3 又は 4 のクレアチニン増加又はコレステロール増加が認められた被験者はいなかった。
- Part 1 では，45 mg 群で最も多く認められた臨床的な意義があると判断したバイタルサインは，7%超の体重増加であり，その割合はプラセボ群（4.5%）と比較して 45 mg 群（9.1%）で高かった。
- Part 2 では，投与 16 週時までのウパダシチニブ 45 mg 1 日 1 回投与は，全体として安全性リスクを増加させなかった。

<u>結論</u>

第 III 相導入療法試験である M14-234 試験 SS 2 において，導入療法としてのウパダシチニブ 45 mg 1 日 1 回，8 週間の投与は，主要評価項目の臨床的寛解率及びすべての順位付き副次評価項目で，プラセボと比較して統計学的に有意に高い改善効果を示した。また，疾患活動性及び症状，内視鏡的及び組織学的評価，炎症のバイオマーカー並びに QOL に関する評価項目でも，ウパダシチニブの有効性が示された。

導入療法としてのウパダシチニブ 45 mg 1 日 1 回投与は，おおむね安全で忍容性は良好であった。ウパダシチニブの既知の安全性プロファイルと比較して，新たな安全性のリスクは認められなかった。

本試験の結果は，中等症から重症の活動性 UC 患者を対象とした導入療法として，ウパダシチニブ 45 mg 1 日 1 回投与を裏付けるものであった。

日本人部分集団の有害事象

日本人部分集団の有害事象の発現状況を以下に示す。

Part 1

有害事象の発現割合は，45 mg 群で 56.4%（31/55 例），プラセボ群で 43.5%（10/23 例）であった。多く認められた（発現割合が 5%以上）有害事象は，45 mg 群で上咽頭炎，貧血，便秘及び好中球数減少であり，プラセボ群で潰瘍性大腸炎，貧血及びそう痒症であった。

治験薬と関連ありの有害事象の発現割合は，45 mg 群で 32.7%（18 例），プラセボ群で 13.0%（3 例）であった。多く認められた（発現割合が 5%以上）治験薬と関連ありの有害事象は，45 mg 群で好中球数減少であり，プラセボ群で潰瘍性大腸炎であった。

高度の有害事象の発現割合は，45 mg 群で 3.6%（2 例），プラセボ群で 13.0%（3 例）であった。45 mg 群で 2 例以上に認められた高度の有害事象はなかった。プラセボ群で 2 例以上に認められた高度の有害事象は，潰瘍性大腸炎であった。

死亡に至った有害事象は認められなかった。

重篤な有害事象の発現割合は，45 mg 群で 7.3%（4 例），プラセボ群で 4.3%（1 例）であった。45 mg 群で 2 例以上に認められた重篤な有害事象はなかった。

治験薬の投与中止に至った有害事象の発現割合は，45 mg 群で 7.3%（4 例），プラセボ群で 8.7%（2 例）であった。45 mg 群で 2 例以上に認められた治験薬の投与中止に至った有害事象はなかった。プラセボ群で 2 例以上に認められた治験薬の投与中止に至った有害事象は，潰瘍性大腸炎であった。

Part 2

有害事象の発現割合は，Part 1 及び Part 2 でウパダシチニブ 45 mg を 1 日 1 回投与した群（以下「45 mg/45 mg 群」）で 42.9%（3/7 例），Part 1 でプラセボ，Part 2 でウパダシチニブ 45 mg を 1 日 1 回投与した群（以下「プラセボ/45 mg 群」）で 53.3%（8/15 例）であった。45 mg/45 mg 群で 2 例以上に認められた有害事象はなかった。プラセボ/45 mg 群で 2 例以上に認められた有害事象は，血中クレアチンホスホキナーゼ増加，発熱及び白血球数減少であった。

治験薬と関連ありの有害事象の発現割合は，45 mg/45 mg 群で 14.3%（1 例），プラセボ/45 mg 群で 33.3%（5 例）であった。プラセボ/45 mg 群で 2 例以上に認められた治験薬と関連ありの有害事象は，白血球数減少であった。

高度の有害事象は認められなかった。

死亡に至った有害事象は認められなかった。

重篤な有害事象は認められなかった。

治験薬の投与中止に至った有害事象は，45 mg/45 mg 群では認められず，プラセボ/45 mg 群で 6.7%（1 例）に認められた。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団	日本人部分集団
有害事象の概要	表 1 (TABLE 14.3__1.1.1_B)	表 8 (TABLE 14.3__1.1.1_B_J)
すべての有害事象	表 2 (TABLE 14.3__1.2.1.1_B)	表 9 (TABLE 14.3__1.2.1.1_B_J)
治験薬と関連ありの有害事象	表 3 (TABLE 14.3__1.3.1.1_B)	表 10 (TABLE 14.3__1.3.1.1_B_J)
高度の有害事象	表 4 (TABLE 14.3__1.3.3_B)	表 11 (TABLE 14.3__1.3.3_B_J)
死亡に至った有害事象	表 5 (TABLE 14.3__2.3.1_B)	表 12 (TABLE 14.3__2.3.1_B_J)
重篤な有害事象	表 6 (TABLE 14.3__2.1.1_B)	表 13 (TABLE 14.3__2.1.1_B_J)
治験薬の投与中止に至った有害事象	表 7 (TABLE 14.3__2.2.1_B)	表 14 (TABLE 14.3__2.2.1_B_J)

表1

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__1.1.1_B

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1 Population and SA2 Population)

	Part 1			Part 2	
	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Difference UPA - Placebo (95% CI&)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
Subjects with:					
Any adverse event (AE)	96 (61.9)	180 (56.4)	-5.5 (-14.9, 3.9)	51 (60.0)	31 (52.5)
Any AE with reasonable possibility of being related to study drug$	36 (23.2)	88 (27.6)	4.4 (-3.9, 12.6)	27 (31.8)	14 (23.7)
Any severe AE	14 (9.0)	9 (2.8)	-6.2 (-11.1, -1.3)	5 (5.9)	1 (1.7)
Any serious AE	9 (5.8)	8 (2.5)	-3.3 (-7.4, 0.8)	2 (2.4)	2 (3.4)
Any AE leading to discontinuation of study drug	14 (9.0)	6 (1.9)	-7.2 (-11.9, -2.4)	5 (5.9)	0
Any AE leading to death	0	0	0.0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
& 95% CI for treatment difference is based on the normal approximation.

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TABLE 14.3 1.1.1 B

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1 Population and SA2 Population)

	Part 1			Part 2	
	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Difference UPA - Placebo (95% CI&)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
Subjects with:					
Deaths#	0	0	0.0	0	0
Occurring <= 30 days after last dose	0	0	0.0	0	0
Occurring > 30 days after last dose	0	0	0.0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
& 95% CI for treatment difference is based on the normal approximation.

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表2

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 30

TABLE 14.3__1.2.1.1_B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
Any adverse event	96 (61.9)	180 (56.4)	51 (60.0)	31 (52.5)
血液およびリンパ系障害	13 (8.4)	24 (7.5)	10 (11.8)	1 (1.7)
貧血	9 (5.8)	8 (2.5)	7 (8.2)	1 (1.7)
失血性貧血	0	1 (0.3)	1 (1.2)	0
鉄欠乏性貧血	1 (0.6)	2 (0.6)	1 (1.2)	0
白血球増加症	0	1 (0.3)	0	0
白血球減少症	0	4 (1.3)	0	0
リンパ球減少症	1 (0.6)	6 (1.9)	0	0
好中球減少症	1 (0.6)	6 (1.9)	3 (3.5)	0
正球性貧血	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

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TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
心臓障害	3 (1.9)	2 (0.6)	0	0
動悸	2 (1.3)	1 (0.3)	0	0
心膜炎	0	1 (0.3)	0	0
頻脈	1 (0.6)	0	0	0
耳および迷路障害	2 (1.3)	1 (0.3)	1 (1.2)	1 (1.7)
感音性難聴	0	0	1 (1.2)	0
耳不快感	0	1 (0.3)	0	0
突発性難聴	1 (0.6)	0	0	0
耳鳴	0	0	0	1 (1.7)
回転性めまい	1 (0.6)	0	0	0
内分泌障害	0	1 (0.3)	0	0
クッシング様症状	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

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TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
眼障害	0	7 (2.2)	3 (3.5)	1 (1.7)
眼精疲労	0	1 (0.3)	0	0
白内障	0	1 (0.3)	1 (1.2)	0
霰粒腫	0	0	1 (1.2)	0
結膜出血	0	1 (0.3)	0	0
結膜充血	0	0	0	1 (1.7)
ドライアイ	0	1 (0.3)	1 (1.2)	0
眼瞼刺激	0	1 (0.3)	0	0
眼瞼肥厚	0	1 (0.3)	0	0
高眼圧症	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
胃腸障害	29 (18.7)	40 (12.5)	11 (12.9)	6 (10.2)
腹部膨満	0	3 (0.9)	1 (1.2)	0
腹痛	1 (0.6)	4 (1.3)	1 (1.2)	2 (3.4)
下腹部痛	1 (0.6)	0	0	0
上腹部痛	1 (0.6)	4 (1.3)	0	0
無酸症	0	0	0	1 (1.7)
裂肛	0	2 (0.6)	0	0
肛門の炎症	1 (0.6)	0	0	0
アフタ性潰瘍	0	2 (0.6)	0	0
大腸炎	1 (0.6)	0	0	0
潰瘍性大腸炎	21 (13.5)	3 (0.9)	3 (3.5)	2 (3.4)
便秘	0	6 (1.9)	2 (2.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
胃腸障害 (Cont.)				
便意切迫	1 (0.6)	0	0	0
横隔膜ヘルニア	1 (0.6)	0	0	0
下痢	0	1 (0.3)	0	0
消化不良	1 (0.6)	3 (0.9)	0	0
おくび	0	1 (0.3)	0	0
糞塊	1 (0.6)	0	0	0
鼓腸	2 (1.3)	2 (0.6)	0	0
食中毒	0	1 (0.3)	0	0
排便回数増加	0	1 (0.3)	0	0
胃食道逆流性疾患	1 (0.6)	3 (0.9)	0	0
歯肉痛	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
胃腸障害 (Cont.)				
痔核	0	4 (1.3)	2 (2.4)	1 (1.7)
大腸ポリープ	0	1 (0.3)	0	0
口唇水疱	0	0	1 (1.2)	0
口唇乾燥	0	1 (0.3)	0	0
口腔内潰瘍形成	0	0	1 (1.2)	0
悪心	3 (1.9)	4 (1.3)	1 (1.2)	0
嚥下痛	0	1 (0.3)	0	0
口腔内痛	0	1 (0.3)	0	0
膵炎	0	1 (0.3)	0	0
直腸異形成	0	1 (0.3)	0	0
直腸ポリープ	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
胃腸障害 (Cont.)				
口内炎	1 (0.6)	0	0	0
舌潰瘍	0	1 (0.3)	0	1 (1.7)
歯の障害	0	1 (0.3)	0	0
嘔吐	0	2 (0.6)	1 (1.2)	0
一般・全身障害および投与部位の状態	4 (2.6)	22 (6.9)	9 (10.6)	2 (3.4)
医薬品副作用	0	1 (0.3)	0	0
無力症	0	3 (0.9)	1 (1.2)	0
胸部不快感	0	2 (0.6)	1 (1.2)	0
胸痛	1 (0.6)	0	0	1 (1.7)
悪寒	0	2 (0.6)	0	1 (1.7)
顔面浮腫	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
疲労	1 (0.6)	2 (0.6)	0	1 (1.7)
過形成	0	1 (0.3)	0	0
倦怠感	0	3 (0.9)	0	0
小結節	0	1 (0.3)	0	0
非心臓性胸痛	0	0	1 (1.2)	0
末梢性浮腫	0	1 (0.3)	0	0
発熱	2 (1.3)	9 (2.8)	6 (7.1)	0
圧痛	0	1 (0.3)	0	0
肝胆道系障害	1 (0.6)	2 (0.6)	1 (1.2)	1 (1.7)
胆石症	0	1 (0.3)	0	1 (1.7)
胆汁うっ滞	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
肝胆道系障害 (Cont.)				
肝機能異常	0	1 (0.3)	0	0
高トランスアミナーゼ血症	0	0	1 (1.2)	0
免疫系障害	1 (0.6)	0	1 (1.2)	0
過敏症	0	0	1 (1.2)	0
季節性アレルギー	1 (0.6)	0	0	0
感染症および寄生虫症	32 (20.6)	71 (22.3)	21 (24.7)	7 (11.9)
膿瘍	0	1 (0.3)	0	0
虫垂炎	0	2 (0.6)	0	0
無症候性細菌尿	0	1 (0.3)	0	0
気管支炎	0	0	2 (2.4)	0
カンジダ感染	0	0	1 (1.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
感染症および寄生虫症 (Cont.)				
蜂巣炎	2 (1.3)	0	0	0
条虫感染	0	1 (0.3)	0	0
結膜炎	1 (0.6)	0	0	0
膀胱炎	0	1 (0.3)	1 (1.2)	0
爪の皮膚糸状菌症	0	1 (0.3)	0	0
耳感染	2 (1.3)	0	0	1 (1.7)
大腸菌感染	1 (0.6)	0	0	0
毛包炎	1 (0.6)	8 (2.5)	0	0
真菌感染	1 (0.6)	0	0	0
皮膚真菌感染	1 (0.6)	0	1 (1.2)	0
胃腸炎	3 (1.9)	3 (0.9)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
感染症および寄生虫症 (Cont.)				
ノロウイルス性胃腸炎	1 (0.6)	1 (0.3)	0	0
ウイルス性胃腸炎	0	1 (0.3)	0	0
陰部ヘルペス	0	2 (0.6)	0	0
陰部単純ヘルペス	0	0	1 (1.2)	0
歯肉炎	1 (0.6)	1 (0.3)	0	0
単純ヘルペス	0	1 (0.3)	0	0
帯状疱疹	0	1 (0.3)	5 (5.9)	3 (5.1)
インフルエンザ	1 (0.6)	3 (0.9)	1 (1.2)	0
下気道感染	0	0	1 (1.2)	0
筋膿瘍	1 (0.6)	0	0	0
上咽頭炎	6 (3.9)	15 (4.7)	4 (4.7)	1 (1.7)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
感染症および寄生虫症 (Cont.)				
口腔真菌感染	0	1 (0.3)	0	0
口腔ヘルペス	0	4 (1.3)	2 (2.4)	0
真菌性外耳炎	0	1 (0.3)	0	0
中耳炎	0	1 (0.3)	0	0
爪囲炎	0	1 (0.3)	0	0
咽頭炎	1 (0.6)	2 (0.6)	3 (3.5)	1 (1.7)
肺炎	1 (0.6)	2 (0.6)	0	0
膿疱	0	2 (0.6)	0	0
膿疱性皮疹	0	1 (0.3)	0	0
気道感染	0	1 (0.3)	0	0
ウイルス性気道感染	1 (0.6)	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
感染症および寄生虫症 (Cont.)				
副鼻腔炎	0	2 (0.6)	1 (1.2)	1 (1.7)
足部白癬	0	1 (0.3)	0	0
癜風	0	1 (0.3)	0	0
歯感染	0	1 (0.3)	0	0
上気道感染	6 (3.9)	8 (2.5)	0	0
尿路感染	3 (1.9)	3 (0.9)	2 (2.4)	0
膣膿瘍	1 (0.6)	0	0	0
ウイルス感染	0	1 (0.3)	0	0
ウイルス性上気道感染	0	2 (0.6)	0	0
外陰部膣カンジダ症	1 (0.6)	1 (0.3)	0	0
外陰膣真菌感染	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
傷害、中毒および処置合併症	1 (0.6)	7 (2.2)	1 (1.2)	1 (1.7)
挫傷	0	3 (0.9)	0	0
熱疲労	0	0	1 (1.2)	0
損傷	0	1 (0.3)	0	0
靭帯捻挫	0	1 (0.3)	0	0
半月板損傷	0	0	0	1 (1.7)
外傷後頚部症候群	0	1 (0.3)	0	0
皮膚擦過傷	1 (0.6)	0	0	0
皮膚裂傷	0	1 (0.3)	0	0
創合併症	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
臨床検査	19 (12.3)	35 (11.0)	9 (10.6)	7 (11.9)
アラニンアミノトランスフェラーゼ増加	3 (1.9)	4 (1.3)	0	1 (1.7)
αヒドロキシ酪酸脱水素酵素増加	0	1 (0.3)	0	0
アミラーゼ増加	0	1 (0.3)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	4 (2.6)	5 (1.6)	1 (1.2)	1 (1.7)
血中ビリルビン増加	0	2 (0.6)	0	0
血中非抱合ビリルビン増加	0	1 (0.3)	0	0
血中コレステロール減少	0	0	1 (1.2)	0
血中コレステロール増加	0	1 (0.3)	0	1 (1.7)
血中クレアチンホスホキナーゼ増加	3 (1.9)	16 (5.0)	5 (5.9)	4 (6.8)
血中ブドウ糖増加	2 (1.3)	0	0	0
血中鉄減少	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
臨床検査 (Cont.)				
血中乳酸脱水素酵素増加	0	1 (0.3)	0	0
血中マグネシウム減少	0	1 (0.3)	0	0
血中トリグリセリド増加	0	0	0	1 (1.7)
尿中血陽性	0	1 (0.3)	0	0
心雑音	1 (0.6)	0	0	0
尿中結晶陽性	1 (0.6)	0	0	0
γ-グルタミルトランスフェラーゼ増加	3 (1.9)	0	0	0
尿中ブドウ糖陽性	1 (0.6)	0	0	0
ヘモグロビン減少	3 (1.9)	0	0	1 (1.7)
高比重リポ蛋白増加	0	1 (0.3)	0	0
眼圧上昇	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
臨床検査 (Cont.)				
リパーゼ増加	0	1 (0.3)	0	0
肝機能検査値上昇	1 (0.6)	0	0	0
低比重リポ蛋白減少	0	0	1 (1.2)	0
低比重リポ蛋白増加	0	1 (0.3)	0	0
リンパ球数減少	0	3 (0.9)	0	1 (1.7)
リンパ球数増加	0	3 (0.9)	0	0
リンパ球百分率減少	0	2 (0.6)	0	0
リンパ球百分率増加	0	1 (0.3)	0	0
好中球数減少	0	10 (3.1)	2 (2.4)	1 (1.7)
好中球数増加	0	1 (0.3)	0	0
好中球百分率増加	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
臨床検査 (Cont.)				
血小板数増加	0	0	1 (1.2)	0
前立腺特異性抗原増加	0	1 (0.3)	0	0
尿中蛋白陽性	3 (1.9)	0	0	0
尿検査異常	1 (0.6)	0	0	0
尿中ケトン体陽性	1 (0.6)	0	0	0
ビタミンD減少	1 (0.6)	0	0	0
体重減少	1 (0.6)	0	1 (1.2)	0
体重増加	1 (0.6)	0	0	0
白血球数減少	1 (0.6)	5 (1.6)	3 (3.5)	0
白血球数増加	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
代謝および栄養障害	6 (3.9)	6 (1.9)	1 (1.2)	3 (5.1)
食欲減退	1 (0.6)	0	0	0
脱水	1 (0.6)	0	0	0
葉酸欠乏	0	1 (0.3)	0	0
高コレステロール血症	0	0	0	1 (1.7)
高血糖	0	0	1 (1.2)	1 (1.7)
高脂血症	0	1 (0.3)	0	1 (1.7)
高ナトリウム血症	0	0	0	1 (1.7)
高トリグリセリド血症	1 (0.6)	0	0	0
低アルブミン血症	1 (0.6)	1 (0.3)	0	0
低カリウム血症	0	1 (0.3)	0	0
低ナトリウム血症	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
代謝および栄養障害 (Cont.)				
低リン酸血症	0	1 (0.3)	0	0
食欲亢進	0	1 (0.3)	0	0
鉄欠乏	2 (1.3)	0	0	0
ビタミンB12欠乏	0	1 (0.3)	0	0
筋骨格系および結合組織障害	15 (9.7)	20 (6.3)	5 (5.9)	2 (3.4)
関節痛	7 (4.5)	5 (1.6)	0	0
関節炎	1 (0.6)	1 (0.3)	0	0
腸炎性関節炎	0	0	0	1 (1.7)
関節障害	0	1 (0.3)	0	0
背部痛	1 (0.6)	3 (0.9)	1 (1.2)	0
肋軟骨炎	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
筋骨格系および結合組織障害 (Cont.)				
側腹部痛	0	0	0	1 (1.7)
筋痙縮	1 (0.6)	1 (0.3)	2 (2.4)	0
筋緊張	0	1 (0.3)	0	0
筋骨格痛	0	1 (0.3)	0	0
筋骨格硬直	0	1 (0.3)	0	0
筋肉痛	1 (0.6)	1 (0.3)	1 (1.2)	0
筋炎	1 (0.6)	0	0	0
骨減少症	1 (0.6)	0	0	0
骨粗鬆症	0	1 (0.3)	0	0
四肢痛	1 (0.6)	1 (0.3)	2 (2.4)	0
脊椎痛	1 (0.6)	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
筋骨格系および結合組織障害 (Cont.)				
脊椎関節障害	1 (0.6)	1 (0.3)	0	0
腱炎	0	1 (0.3)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	4 (1.3)	0	0
神経節腫	0	1 (0.3)	0	0
皮膚乳頭腫	0	2 (0.6)	0	0
子宮平滑筋腫	0	1 (0.3)	0	0
神経系障害	6 (3.9)	20 (6.3)	7 (8.2)	3 (5.1)
浮動性めまい	0	4 (1.3)	1 (1.2)	0
頭痛	4 (2.6)	13 (4.1)	4 (4.7)	2 (3.4)
片頭痛	1 (0.6)	0	1 (1.2)	0
神経痛	0	0	0	1 (1.7)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
神経系障害 (Cont.)				
錯感覚	0	1 (0.3)	0	0
ヘルペス後神経痛	0	1 (0.3)	0	0
失神寸前の状態	0	1 (0.3)	0	0
坐骨神経痛	0	0	1 (1.2)	0
失神	1 (0.6)	0	0	0
振戦	0	1 (0.3)	0	0
精神障害	5 (3.2)	4 (1.3)	0	2 (3.4)
不安	2 (1.3)	2 (0.6)	0	0
うつ病	1 (0.6)	0	0	0
不眠症	2 (1.3)	1 (0.3)	0	2 (3.4)
睡眠障害	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
腎および尿路障害	3 (1.9)	8 (2.5)	3 (3.5)	0
慢性腎臓病	0	2 (0.6)	0	0
排尿困難	0	1 (0.3)	1 (1.2)	0
血尿	1 (0.6)	0	0	0
白血球尿	0	0	1 (1.2)	0
排尿異常	0	1 (0.3)	0	0
腎結石症	0	1 (0.3)	0	0
頻尿	0	1 (0.3)	0	0
蛋白尿	2 (1.3)	1 (0.3)	0	0
腎仙痛	0	2 (0.6)	0	0
腎臓痛	0	0	1 (1.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
生殖系および乳房障害	0	5 (1.6)	0	0
月経困難症	0	1 (0.3)	0	0
不規則月経	0	1 (0.3)	0	0
精液変色	0	1 (0.3)	0	0
精嚢腺炎	0	1 (0.3)	0	0
外陰腟不快感	0	1 (0.3)	0	0
呼吸器、胸郭および縦隔障害	7 (4.5)	18 (5.6)	4 (4.7)	2 (3.4)
胞隔炎	0	0	1 (1.2)	0
カタル	1 (0.6)	0	0	0
咳嗽	2 (1.3)	5 (1.6)	2 (2.4)	1 (1.7)
嚢胞性肺疾患	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
咽喉乾燥	0	1 (0.3)	0	0
呼吸困難	0	2 (0.6)	0	0
鼻閉	0	0	1 (1.2)	0
口腔咽頭痛	1 (0.6)	6 (1.9)	1 (1.2)	0
咽頭紅斑	0	1 (0.3)	0	0
胸膜障害	1 (0.6)	0	0	0
肺臓炎	1 (0.6)	0	0	0
湿性咳嗽	0	1 (0.3)	0	0
肺腫瘤	2 (1.3)	1 (0.3)	0	0
気道うっ血	0	1 (0.3)	0	0
アレルギー性鼻炎	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
副鼻腔うっ血	0	0	0	1 (1.7)
副鼻腔障害	0	1 (0.3)	0	0
上気道の炎症	1 (0.6)	0	0	0
皮膚および皮下組織障害	9 (5.8)	37 (11.6)	8 (9.4)	6 (10.2)
ざ瘡	1 (0.6)	15 (4.7)	2 (2.4)	1 (1.7)
脱毛症	0	1 (0.3)	3 (3.5)	2 (3.4)
皮膚炎	0	0	0	1 (1.7)
ざ瘡様皮膚炎	1 (0.6)	4 (1.3)	0	0
皮膚乾燥	1 (0.6)	0	0	0
異汗性湿疹	1 (0.6)	0	0	0
斑状出血	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
皮膚および皮下組織障害 (Cont.)				
湿疹	1 (0.6)	1 (0.3)	1 (1.2)	0
多形紅斑	0	1 (0.3)	0	0
過角化	0	1 (0.3)	0	0
嵌入爪	0	0	0	1 (1.7)
皮膚疼痛	0	1 (0.3)	0	0
丘疹	0	3 (0.9)	1 (1.2)	0
光線過敏性反応	0	0	0	1 (1.7)
そう痒症	4 (2.6)	1 (0.3)	0	0
発疹	1 (0.6)	8 (2.5)	0	1 (1.7)
斑状皮疹	0	1 (0.3)	0	0
丘疹性皮疹	0	2 (0.6)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
皮膚および皮下組織障害 (Cont.)				
脂漏性皮膚炎	0	1 (0.3)	0	0
皮膚変色	0	1 (0.3)	0	0
皮膚剥脱	0	1 (0.3)	0	0
皮膚病変	0	0	1 (1.2)	0
皮膚線条	0	1 (0.3)	0	0
血管障害	4 (2.6)	7 (2.2)	1 (1.2)	2 (3.4)
動脈硬化症	0	1 (0.3)	0	0
高血圧	2 (1.3)	5 (1.6)	1 (1.2)	1 (1.7)
低血圧	0	0	0	1 (1.7)
末梢冷感	1 (0.6)	0	0	0
レイノー現象	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
血管障害 (Cont.)				
表在性血栓性静脈炎	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表3

TABLE 14.3__1.3.1.1_B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
Any adverse event	36 (23.2)	88 (27.6)	27 (31.8)	14 (23.7)
血液およびリンパ系障害	2 (1.3)	13 (4.1)	4 (4.7)	1 (1.7)
貧血	0	1 (0.3)	1 (1.2)	1 (1.7)
失血性貧血	0	0	1 (1.2)	0
鉄欠乏性貧血	0	0	1 (1.2)	0
白血球増加症	0	1 (0.3)	0	0
白血球減少症	0	4 (1.3)	0	0
リンパ球減少症	1 (0.6)	3 (0.9)	0	0
好中球減少症	1 (0.6)	6 (1.9)	3 (3.5)	0
心臓障害	1 (0.6)	0	0	0
頻脈	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
耳および迷路障害	0	0	0	1 (1.7)
耳鳴	0	0	0	1 (1.7)
眼障害	0	1 (0.3)	1 (1.2)	0
霰粒腫	0	0	1 (1.2)	0
ドライアイ	0	1 (0.3)	0	0
胃腸障害	13 (8.4)	13 (4.1)	2 (2.4)	1 (1.7)
腹部膨満	0	1 (0.3)	0	0
腹痛	0	0	0	1 (1.7)
上腹部痛	1 (0.6)	1 (0.3)	0	0
アフタ性潰瘍	0	1 (0.3)	0	0
潰瘍性大腸炎	11 (7.1)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
胃腸障害 (Cont.)				
便秘	0	4 (1.3)	1 (1.2)	0
便意切迫	1 (0.6)	0	0	0
消化不良	0	1 (0.3)	0	0
おくび	0	1 (0.3)	0	0
鼓腸	1 (0.6)	1 (0.3)	0	0
胃食道逆流性疾患	0	1 (0.3)	0	0
歯肉痛	0	1 (0.3)	0	0
口唇水疱	0	0	1 (1.2)	0
悪心	0	1 (0.3)	0	0
口腔内痛	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
一般・全身障害および投与部位の状態	1 (0.6)	10 (3.1)	0	2 (3.4)
無力症	0	1 (0.3)	0	0
胸部不快感	0	2 (0.6)	0	0
胸痛	1 (0.6)	0	0	1 (1.7)
悪寒	0	0	0	1 (1.7)
疲労	0	1 (0.3)	0	1 (1.7)
過形成	0	1 (0.3)	0	0
倦怠感	0	3 (0.9)	0	0
末梢性浮腫	0	1 (0.3)	0	0
発熱	0	3 (0.9)	0	0
肝胆道系障害	0	0	1 (1.2)	1 (1.7)
胆石症	0	0	0	1 (1.7)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
肝胆道系障害 (Cont.)				
高トランスアミナーゼ血症	0	0	1 (1.2)	0
感染症および寄生虫症	6 (3.9)	29 (9.1)	12 (14.1)	3 (5.1)
膿瘍	0	1 (0.3)	0	0
虫垂炎	0	1 (0.3)	0	0
無症候性細菌尿	0	1 (0.3)	0	0
気管支炎	0	0	1 (1.2)	0
条虫感染	0	1 (0.3)	0	0
膀胱炎	0	1 (0.3)	0	0
爪の皮膚糸状菌症	0	1 (0.3)	0	0
毛包炎	0	5 (1.6)	0	0
真菌感染	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
感染症および寄生虫症 (Cont.)				
皮膚真菌感染	0	0	1 (1.2)	0
陰部ヘルペス	0	1 (0.3)	0	0
陰部単純ヘルペス	0	0	1 (1.2)	0
歯肉炎	1 (0.6)	0	0	0
単純ヘルペス	0	1 (0.3)	0	0
帯状疱疹	0	1 (0.3)	5 (5.9)	2 (3.4)
インフルエンザ	0	1 (0.3)	0	0
上咽頭炎	1 (0.6)	2 (0.6)	3 (3.5)	0
口腔ヘルペス	0	2 (0.6)	0	0
真菌性外耳炎	0	1 (0.3)	0	0
爪囲炎	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
感染症および寄生虫症 (Cont.)				
咽頭炎	0	1 (0.3)	1 (1.2)	0
肺炎	0	2 (0.6)	0	0
膿疱性皮疹	0	1 (0.3)	0	0
副鼻腔炎	0	1 (0.3)	0	1 (1.7)
足部白癬	0	1 (0.3)	0	0
癜風	0	1 (0.3)	0	0
上気道感染	2 (1.3)	3 (0.9)	0	0
尿路感染	1 (0.6)	0	1 (1.2)	0
ウイルス感染	0	1 (0.3)	0	0
ウイルス性上気道感染	0	2 (0.6)	0	0
外陰部腟カンジダ症	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
臨床検査	6 (3.9)	29 (9.1)	5 (5.9)	5 (8.5)
アラニンアミノトランスフェラーゼ増加	1 (0.6)	4 (1.3)	0	1 (1.7)
αヒドロキシ酪酸脱水素酵素増加	0	1 (0.3)	0	0
アミラーゼ増加	0	1 (0.3)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.6)	4 (1.3)	0	1 (1.7)
血中ビリルビン増加	0	1 (0.3)	0	0
血中コレステロール増加	0	1 (0.3)	0	0
血中クレアチンホスホキナーゼ増加	1 (0.6)	13 (4.1)	2 (2.4)	4 (6.8)
血中乳酸脱水素酵素増加	0	1 (0.3)	0	0
血中トリグリセリド増加	0	0	0	1 (1.7)
尿中結晶陽性	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
臨床検査 (Cont.)				
高比重リポ蛋白増加	0	1 (0.3)	0	0
肝機能検査値上昇	1 (0.6)	0	0	0
低比重リポ蛋白増加	0	1 (0.3)	0	0
リンパ球数減少	0	2 (0.6)	0	1 (1.7)
リンパ球数増加	0	2 (0.6)	0	0
リンパ球百分率減少	0	2 (0.6)	0	0
好中球数減少	0	10 (3.1)	2 (2.4)	1 (1.7)
好中球数増加	0	1 (0.3)	0	0
好中球百分率増加	0	1 (0.3)	0	0
尿中蛋白陽性	1 (0.6)	0	0	0
白血球数減少	1 (0.6)	5 (1.6)	3 (3.5)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
代謝および栄養障害	0	2 (0.6)	1 (1.2)	3 (5.1)
高コレステロール血症	0	0	0	1 (1.7)
高血糖	0	0	1 (1.2)	1 (1.7)
高脂血症	0	1 (0.3)	0	1 (1.7)
食欲亢進	0	1 (0.3)	0	0
筋骨格系および結合組織障害	3 (1.9)	3 (0.9)	2 (2.4)	0
関節痛	1 (0.6)	1 (0.3)	0	0
筋痙縮	1 (0.6)	0	1 (1.2)	0
筋緊張	0	1 (0.3)	0	0
筋肉痛	0	1 (0.3)	0	0
四肢痛	1 (0.6)	0	1 (1.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (0.3)	0	0
皮膚乳頭腫	0	1 (0.3)	0	0
神経系障害	4 (2.6)	8 (2.5)	1 (1.2)	1 (1.7)
浮動性めまい	0	3 (0.9)	1 (1.2)	0
頭痛	3 (1.9)	5 (1.6)	0	1 (1.7)
片頭痛	1 (0.6)	0	0	0
ヘルペス後神経痛	0	1 (0.3)	0	0
精神障害	0	1 (0.3)	0	0
不眠症	0	1 (0.3)	0	0
腎および尿路障害	2 (1.3)	3 (0.9)	1 (1.2)	0
慢性腎臓病	0	2 (0.6)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
腎および尿路障害 (Cont.)				
排尿困難	0	1 (0.3)	0	0
白血球尿	0	0	1 (1.2)	0
蛋白尿	2 (1.3)	0	0	0
生殖系および乳房障害	0	2 (0.6)	0	0
不規則月経	0	1 (0.3)	0	0
精液変色	0	1 (0.3)	0	0
呼吸器、胸郭および縦隔障害	0	3 (0.9)	0	2 (3.4)
咳嗽	0	1 (0.3)	0	1 (1.7)
口腔咽頭痛	0	1 (0.3)	0	0
気道うっ血	0	1 (0.3)	0	0
副鼻腔うっ血	0	0	0	1 (1.7)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
副鼻腔障害	0	1 (0.3)	0	0
皮膚および皮下組織障害	3 (1.9)	20 (6.3)	4 (4.7)	2 (3.4)
ざ瘡	1 (0.6)	9 (2.8)	0	0
脱毛症	0	1 (0.3)	2 (2.4)	1 (1.7)
ざ瘡様皮膚炎	0	1 (0.3)	0	0
湿疹	0	1 (0.3)	0	0
過角化	0	1 (0.3)	0	0
皮膚疼痛	0	1 (0.3)	0	0
丘疹	0	3 (0.9)	1 (1.2)	0
そう痒症	2 (1.3)	0	0	0
発疹	1 (0.6)	4 (1.3)	0	1 (1.7)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
皮膚および皮下組織障害 (Cont.)				
斑状皮疹	0	1 (0.3)	0	0
丘疹性皮疹	0	2 (0.6)	0	0
皮膚剥脱	0	1 (0.3)	0	0
皮膚病変	0	0	1 (1.2)	0
皮膚線条	0	1 (0.3)	0	0
血管障害	1 (0.6)	1 (0.3)	1 (1.2)	0
高血圧	1 (0.6)	1 (0.3)	1 (1.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表4

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL

TABLE 14.3__1.3.3_B

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
Any adverse event	14 (9.0)	9 (2.8)	5 (5.9)	1 (1.7)
血液およびリンパ系障害	1 (0.6)	2 (0.6)	1 (1.2)	0
貧血	1 (0.6)	0	1 (1.2)	0
リンパ球減少症	0	2 (0.6)	0	0
胃腸障害	11 (7.1)	3 (0.9)	1 (1.2)	1 (1.7)
腹痛	0	1 (0.3)	0	0
大腸炎	1 (0.6)	0	0	0
潰瘍性大腸炎	9 (5.8)	2 (0.6)	1 (1.2)	1 (1.7)
鼓腸	1 (0.6)	0	0	0
感染症および寄生虫症	1 (0.6)	2 (0.6)	1 (1.2)	0
虫垂炎	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3 B

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
感染症および寄生虫症 (Cont.)				
蜂巣炎	1 (0.6)	0	0	0
ノロウイルス性胃腸炎	0	1 (0.3)	0	0
帯状疱疹	0	0	1 (1.2)	0
臨床検査	2 (1.3)	3 (0.9)	1 (1.2)	0
アミラーゼ増加	0	1 (0.3)	0	0
血中クレアチンホスホキナーゼ増加	1 (0.6)	1 (0.3)	0	0
ヘモグロビン減少	1 (0.6)	0	0	0
好中球数減少	0	1 (0.3)	1 (1.2)	0
白血球数増加	0	1 (0.3)	0	0
代謝および栄養障害	1 (0.6)	1 (0.3)	0	0
低アルブミン血症	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3 B

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=155) n (%)	Part 1 UPA 45 mg QD (N=319) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=85) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
代謝および栄養障害 (Cont.)				
低リン酸血症	0	1 (0.3)	0	0
皮膚および皮下組織障害	0	1 (0.3)	1 (1.2)	0
湿疹	0	0	1 (1.2)	0
多形紅斑	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表5

[redacted]20[redacted] 10:50 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.3.1_B

Subjects with Treatment-Emergent Adverse Events Leading to Death
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
Any adverse event	0	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表6

[redacted]20[redacted] 10:50 <[redacted] >
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL

TABLE 14.3__2.1.1_B

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
Any adverse event	9 (5.8)	8 (2.5)	2 (2.4)	2 (3.4)
血液およびリンパ系障害	0	0	2 (2.4)	0
貧血	0	0	2 (2.4)	0
胃腸障害	6 (3.9)	2 (0.6)	1 (1.2)	1 (1.7)
大腸炎	1 (0.6)	0	0	0
潰瘍性大腸炎	5 (3.2)	2 (0.6)	1 (1.2)	1 (1.7)
横隔膜ヘルニア	1 (0.6)	0	0	0
一般・全身障害および投与部位の状態	0	1 (0.3)	0	0
発熱	0	1 (0.3)	0	0
感染症および寄生虫症	2 (1.3)	5 (1.6)	0	0
虫垂炎	0	2 (0.6)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.1.1 B

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
感染症および寄生虫症 (Cont.)				
蜂巣炎	1 (0.6)	0	0	0
ノロウイルス性胃腸炎	0	1 (0.3)	0	0
筋膿瘍	1 (0.6)	0	0	0
肺炎	0	1 (0.3)	0	0
ウイルス感染	0	1 (0.3)	0	0
代謝および栄養障害	1 (0.6)	0	0	0
低アルブミン血症	1 (0.6)	0	0	0
血管障害	0	0	0	1 (1.7)
低血圧	0	0	0	1 (1.7)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表7

[redacted]20[redacted] 10:50 <[redacted] >
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__2.2.1_B

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
Any adverse event	14 (9.0)	6 (1.9)	5 (5.9)	0
胃腸障害	12 (7.7)	3 (0.9)	1 (1.2)	0
大腸炎	1 (0.6)	0	0	0
潰瘍性大腸炎	11 (7.1)	2 (0.6)	1 (1.2)	0
直腸異形成	0	1 (0.3)	0	0
一般・全身障害および投与部位の状態	0	1 (0.3)	0	0
発熱	0	1 (0.3)	0	0
感染症および寄生虫症	1 (0.6)	2 (0.6)	2 (2.4)	0
帯状疱疹	0	1 (0.3)	2 (2.4)	0
筋膿瘍	1 (0.6)	0	0	0
ウイルス感染	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.2.1 B

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=155) n (%)	UPA 45 mg QD (N=319) n (%)	Placebo/ UPA 45 mg QD (N=85) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=59) n (%)
臨床検査	1 (0.6)	0	1 (1.2)	0
血中クレアチンホスホキナーゼ増加	0	0	1 (1.2)	0
ヘモグロビン減少	1 (0.6)	0	0	0
腎および尿路障害	0	1 (0.3)	0	0
慢性腎臓病	0	1 (0.3)	0	0
呼吸器、胸郭および縦隔障害	0	0	1 (1.2)	0
胞隔炎	0	0	1 (1.2)	0
皮膚および皮下組織障害	1 (0.6)	0	0	0
そう痒症	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表8

[redacted]20[redacted] 09:39 <[redacted] >
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__1.1.1_B_J

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1			Part 2	
	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Difference UPA - Placebo (95% CI&)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Subjects with:					
Any adverse event (AE)	10 (43.5)	31 (56.4)	12.9 (-11.2, 37.0)	8 (53.3)	3 (42.9)
Any AE with reasonable possibility of being related to study drug$	3 (13.0)	18 (32.7)	19.7 (1.2, 38.2)	5 (33.3)	1 (14.3)
Any severe AE	3 (13.0)	2 (3.6)	-9.4 (-24.0, 5.2)	0	0
Any serious AE	1 (4.3)	4 (7.3)	2.9 (-7.9, 13.7)	0	0
Any AE leading to discontinuation of study drug	2 (8.7)	4 (7.3)	-1.4 (-14.8, 12.0)	1 (6.7)	0
Any AE leading to death	0	0	0.0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
& 95% CI for treatment difference is based on the normal approximation.

Program Source Code: [redacted]

TABLE 14.3 1.1.1 B J

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1			Part 2	
	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Difference UPA - Placebo (95% CI&)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Subjects with:					
Deaths#	0	0	0.0	0	0
Occurring <= 30 days after last dose	0	0	0.0	0	0
Occurring > 30 days after last dose	0	0	0.0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
& 95% CI for treatment difference is based on the normal approximation.

Program Source Code: [redacted]

表9

[redacted]20[redacted] 10:23 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 8

TABLE 14.3__1.2.1.1_B_J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	10 (43.5)	31 (56.4)	8 (53.3)	3 (42.9)
血液およびリンパ系障害	2 (8.7)	8 (14.5)	2 (13.3)	0
貧血	2 (8.7)	3 (5.5)	1 (6.7)	0
鉄欠乏性貧血	0	1 (1.8)	0	0
白血球減少症	0	2 (3.6)	0	0
リンパ球減少症	0	2 (3.6)	0	0
好中球減少症	0	2 (3.6)	1 (6.7)	0
胃腸障害	4 (17.4)	6 (10.9)	1 (6.7)	0
腹部膨満	0	0	1 (6.7)	0
肛門の炎症	1 (4.3)	0	0	0
潰瘍性大腸炎	3 (13.0)	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=23) n (%)	Part 1 UPA 45 mg QD (N=55) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=15) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
胃腸障害 (Cont.)				
便秘	0	3 (5.5)	0	0
痔核	0	1 (1.8)	0	0
口唇乾燥	0	1 (1.8)	0	0
悪心	1 (4.3)	1 (1.8)	0	0
膵炎	0	1 (1.8)	0	0
一般・全身障害および投与部位の状態	1 (4.3)	2 (3.6)	2 (13.3)	0
医薬品副作用	0	1 (1.8)	0	0
倦怠感	0	1 (1.8)	0	0
発熱	1 (4.3)	1 (1.8)	2 (13.3)	0
肝胆道系障害	0	1 (1.8)	0	0
肝機能異常	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
感染症および寄生虫症	2 (8.7)	12 (21.8)	3 (20.0)	1 (14.3)
虫垂炎	0	1 (1.8)	0	0
無症候性細菌尿	0	1 (1.8)	0	0
膀胱炎	0	1 (1.8)	0	0
毛包炎	0	1 (1.8)	0	0
胃腸炎	0	1 (1.8)	0	0
帯状疱疹	0	1 (1.8)	1 (6.7)	1 (14.3)
上咽頭炎	1 (4.3)	6 (10.9)	1 (6.7)	0
口腔ヘルペス	0	0	1 (6.7)	0
上気道感染	1 (4.3)	1 (1.8)	0	0
ウイルス感染	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=23) n (%)	Part 1 UPA 45 mg QD (N=55) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=15) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
感染症および寄生虫症 (Cont.)				
外陰部腟カンジダ症	0	1 (1.8)	0	0
傷害、中毒および処置合併症	0	1 (1.8)	0	0
皮膚裂傷	0	1 (1.8)	0	0
臨床検査	1 (4.3)	7 (12.7)	5 (33.3)	0
アラニンアミノトランスフェラーゼ増加	0	1 (1.8)	0	0
アミラーゼ増加	0	1 (1.8)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (1.8)	1 (6.7)	0
血中クレアチンホスホキナーゼ増加	0	1 (1.8)	4 (26.7)	0
尿中血陽性	0	1 (1.8)	0	0
リパーゼ増加	0	1 (1.8)	0	0
リンパ球数減少	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=23) n (%)	Part 1 UPA 45 mg QD (N=55) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=15) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
臨床検査 (Cont.)				
リンパ球数増加	0	2 (3.6)	0	0
リンパ球百分率増加	0	1 (1.8)	0	0
好中球数減少	0	3 (5.5)	1 (6.7)	0
前立腺特異性抗原増加	0	1 (1.8)	0	0
体重減少	1 (4.3)	0	0	0
白血球数減少	0	2 (3.6)	2 (13.3)	0
白血球数増加	0	1 (1.8)	0	0
代謝および栄養障害	1 (4.3)	0	0	0
食欲減退	1 (4.3)	0	0	0
低アルブミン血症	1 (4.3)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
筋骨格系および結合組織障害	1 (4.3)	2 (3.6)	0	0
関節痛	1 (4.3)	0	0	0
関節障害	0	1 (1.8)	0	0
筋骨格硬直	0	1 (1.8)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (1.8)	0	0
子宮平滑筋腫	0	1 (1.8)	0	0
神経系障害	0	4 (7.3)	1 (6.7)	0
浮動性めまい	0	1 (1.8)	0	0
頭痛	0	1 (1.8)	1 (6.7)	0
ヘルペス後神経痛	0	1 (1.8)	0	0
失神寸前の状態	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
精神障害	1 (4.3)	0	0	0
不眠症	1 (4.3)	0	0	0
腎および尿路障害	0	2 (3.6)	0	0
慢性腎臓病	0	1 (1.8)	0	0
蛋白尿	0	1 (1.8)	0	0
呼吸器、胸郭および縦隔障害	1 (4.3)	2 (3.6)	0	1 (14.3)
咳嗽	0	0	0	1 (14.3)
口腔咽頭痛	0	2 (3.6)	0	0
上気道の炎症	1 (4.3)	0	0	0
皮膚および皮下組織障害	4 (17.4)	6 (10.9)	0	0
ざ瘡	0	2 (3.6)	0	0
脱毛症	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 B J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=23) n (%)	Part 1 UPA 45 mg QD (N=55) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=15) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
皮膚および皮下組織障害 (Cont.)				
ざ瘡様皮膚炎	0	1 (1.8)	0	0
皮膚乾燥	1 (4.3)	0	0	0
湿疹	1 (4.3)	1 (1.8)	0	0
多形紅斑	0	1 (1.8)	0	0
皮膚疼痛	0	1 (1.8)	0	0
そう痒症	2 (8.7)	0	0	0
血管障害	1 (4.3)	0	0	1 (14.3)
高血圧	0	0	0	1 (14.3)
末梢冷感	1 (4.3)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表10

TABLE 14.3__1.3.1.1_B_J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	3 (13.0)	18 (32.7)	5 (33.3)	1 (14.3)
血液およびリンパ系障害	0	4 (7.3)	1 (6.7)	0
貧血	0	1 (1.8)	0	0
白血球減少症	0	2 (3.6)	0	0
リンパ球減少症	0	1 (1.8)	0	0
好中球減少症	0	2 (3.6)	1 (6.7)	0
胃腸障害	3 (13.0)	2 (3.6)	0	0
潰瘍性大腸炎	3 (13.0)	0	0	0
便秘	0	2 (3.6)	0	0
一般・全身障害および投与部位の状態	0	1 (1.8)	0	0
倦怠感	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=23) n (%)	Part 1 UPA 45 mg QD (N=55) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=15) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
発熱	0	1 (1.8)	0	0
感染症および寄生虫症	0	5 (9.1)	2 (13.3)	0
虫垂炎	0	1 (1.8)	0	0
無症候性細菌尿	0	1 (1.8)	0	0
膀胱炎	0	1 (1.8)	0	0
毛包炎	0	1 (1.8)	0	0
帯状疱疹	0	1 (1.8)	1 (6.7)	0
上咽頭炎	0	0	1 (6.7)	0
ウイルス感染	0	1 (1.8)	0	0
外陰部腟カンジダ症	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=23) n (%)	Part 1 UPA 45 mg QD (N=55) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=15) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
臨床検査	0	7 (12.7)	3 (20.0)	0
アラニンアミノトランスフェラーゼ増加	0	1 (1.8)	0	0
アミラーゼ増加	0	1 (1.8)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (1.8)	0	0
血中クレアチンホスホキナーゼ増加	0	1 (1.8)	1 (6.7)	0
リンパ球数減少	0	1 (1.8)	0	0
リンパ球数増加	0	1 (1.8)	0	0
好中球数減少	0	3 (5.5)	1 (6.7)	0
白血球数減少	0	2 (3.6)	2 (13.3)	0
神経系障害	0	1 (1.8)	0	0
ヘルペス後神経痛	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 B J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
腎および尿路障害	0	1 (1.8)	0	0
慢性腎臓病	0	1 (1.8)	0	0
呼吸器、胸郭および縦隔障害	0	0	0	1 (14.3)
咳嗽	0	0	0	1 (14.3)
皮膚および皮下組織障害	0	5 (9.1)	0	0
ざ瘡	0	2 (3.6)	0	0
脱毛症	0	1 (1.8)	0	0
ざ瘡様皮膚炎	0	1 (1.8)	0	0
湿疹	0	1 (1.8)	0	0
皮膚疼痛	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表11

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
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TABLE 14.3__1.3.3_B_J

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	3 (13.0)	2 (3.6)	0	0
血液およびリンパ系障害	1 (4.3)	1 (1.8)	0	0
貧血	1 (4.3)	0	0	0
リンパ球減少症	0	1 (1.8)	0	0
胃腸障害	2 (8.7)	1 (1.8)	0	0
潰瘍性大腸炎	2 (8.7)	1 (1.8)	0	0
臨床検査	0	1 (1.8)	0	0
アミラーゼ増加	0	1 (1.8)	0	0
白血球数増加	0	1 (1.8)	0	0
代謝および栄養障害	1 (4.3)	0	0	0
低アルブミン血症	1 (4.3)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3 B J

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=23) n (%)	Part 1 UPA 45 mg QD (N=55) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=15) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
皮膚および皮下組織障害	0	1 (1.8)	0	0
多形紅斑	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表12

[redacted]20[redacted] 10:23 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.3.1_B_J

Subjects with Treatment-Emergent Adverse Events Leading to Death
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	0	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表13

[redacted]20[redacted] 10:23 <[redacted] >
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.1.1_B_J

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	1 (4.3)	4 (7.3)	0	0
胃腸障害	0	1 (1.8)	0	0
潰瘍性大腸炎	0	1 (1.8)	0	0
一般・全身障害および投与部位の状態	0	1 (1.8)	0	0
発熱	0	1 (1.8)	0	0
感染症および寄生虫症	0	2 (3.6)	0	0
虫垂炎	0	1 (1.8)	0	0
ウイルス感染	0	1 (1.8)	0	0
代謝および栄養障害	1 (4.3)	0	0	0
低アルブミン血症	1 (4.3)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表14

[redacted]20[redacted] 10:23 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.2.1_B_J

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=23) n (%)	UPA 45 mg QD (N=55) n (%)	Placebo/ UPA 45 mg QD (N=15) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	2 (8.7)	4 (7.3)	1 (6.7)	0
胃腸障害	2 (8.7)	1 (1.8)	0	0
潰瘍性大腸炎	2 (8.7)	1 (1.8)	0	0
一般・全身障害および投与部位の状態	0	1 (1.8)	0	0
発熱	0	1 (1.8)	0	0
感染症および寄生虫症	0	2 (3.6)	1 (6.7)	0
帯状疱疹	0	1 (1.8)	1 (6.7)	0
ウイルス感染	0	1 (1.8)	0	0
腎および尿路障害	0	1 (1.8)	0	0
慢性腎臓病	0	1 (1.8)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo	3[redacted]	MALE	ASIAN

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
FATIGUE	20[redacted]
HEADACHES	19[redacted]
RECTAL BLEEDING	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo			[redacted]20[redacted] / 1	[redacted]20[redacted] / 15	15

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -230
HYDROCORTISONE	10 %	OTHER: Q12 HOURS	Y-M: 20[redacted] / -106
MESALAZINE	1000 mg	BID	Y-M: 20[redacted] / -106
METHOCARBAMOL;PARACETAMOL	2 OTHER: TABLETS	PRN	Y-M: 20[redacted] / -121
CALCIUM CARBONATE	1500 mg	QD	Y-M: 20[redacted] / -41
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted] / -41
PREDNISONE	25 mg	QD	Y-M: 20[redacted] / -41
MIDAZOLAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / -14
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -14
PROPOFOL	100 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / -14
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	4 L	OTHER: ONCE	Y-M: 20[redacted] / -15
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / -19
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -27
PARACETAMOL	1000 mg	PRN	Y: 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
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 15
METHOCARBAMOL;PARACETAMOL	2 OTHER: TABLETS	PRN	Y-M: 20[redacted] / -121	ONGOING
CALCIUM CARBONATE	1500 mg	QD	Y-M: 20[redacted] / -41	Y-M: 20[redacted] / 15
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted] / -41	Y-M: 20[redacted] / 15
MIDAZOLAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / -14
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 13
PROPOFOL	100 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / -14

MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	4 L	OTHER: ONCE	Y-M: 20[redacted] / -15	Y-M: 20[redacted] / -14
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / -19	Y-M: 20[redacted] / -15
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -27	Y-M: 20[redacted] / -20
TINZAPARIN	4500 IU	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 22
CALCIUM	500 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 23
CIPROFLOXACIN	500 mg	OTHER: Q12HRS	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 19
METHYLPREDNISOLONE	30 mg	BID	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 19
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 19
PROPOFOL	150 mg	OTHER: ONCE	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 16
VITAMIN D NOS	1000 IU	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 23
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 21
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 32
PARACETAMOL	1000 mg	PRN	Y: 20[redacted]	ONGOING

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

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 7
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 12): STOOL NPTST124-CLOSTRIDIUM DIFFICILE TEST: NEGATIVE; [redacted]20[redacted] (RX DAY 17): STOOL NPTST124-CLOSTRIDIUM DIFFICILE TEST: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY -15): COLONOSCOPY: MODERATE TO SEVERE COLITIS, MAYO 2 ON THE RIGHT SIDE AND MAYO SCORE 3 ON THE LEFT COLON, SIGMOID AND RECTUM; [redacted]20[redacted] (RX DAY 16): COLONOSCOPY: MODERATE TO SEVERE COLITIS, MAYO 2 ON THE RIGHT COLON AND MAYO SCORE 3 ON THE LEFT COLON, SIGMOID AND RECTUM

AE Stopped Rx Day	22 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	16 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES

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

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はカナダの 3[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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），直腸出血，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与7日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。

事象の発現前，被験者は 投与43日前＊　に夜間の症状として，8–10 回の血便を経験した。

投与7日後＊　，被験者は腹痛を経験し始め，血便は 1 日 10–15 日に増えた。 投与15日後＊，被験者は入院した。投与17日後＊　，被験者は結腸内視鏡検査を受けた。 投与22日後＊，被験者は退院した。治験責任医師によると，治験薬の投与は有効性が認められないため中止された。

投与された薬剤は，ソル・メドロール，イムラン及び prednisone であった。

The patient's past medications include:

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

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

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

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

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

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

SALOFALK SUPPOSITORY for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

---

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Not Applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE TEST:** NEGATIVE

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE TEST:** NEGATIVE

[redacted] **20[redacted] COLONOSCOPY:** Moderate to severe colitis, Mayo 2 on the right side and Mayo Score 3 on the left colon, sigmoid and rectum

[redacted] **20[redacted] COLONOSCOPY:** 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
ノロウイルス性胃腸炎	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 45 mg /P2:ABT-494 45 mg	2[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
GALLSTONE PANCREATITIS	20[redacted]
PRIMARY SCLEROSING CHOLANGITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 57	2[redacted]20[redacted] / 113	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]-[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
URSODEOXYCHOLIC ACID	500 mg	BID	Y-M: 20[redacted]-[redacted]
PREDNISONE	15 mg	QD	Y-M: 20[redacted]-[redacted] / -11
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -18
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	4 L	OTHER: AS DIRECTED	Y-M: 20[redacted]-[redacted] / -20

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
URSODEOXYCHOLIC ACID	500 mg	BID	Y-M: 20[redacted]-09	ONGOING
PREDNISONE	15 mg	QD	Y-M: 20[redacted]-[redacted] / -11	ONGOING
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -18	Y-M: 20[redacted]-[redacted] / -12
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	4 L	OTHER: AS DIRECTED	Y-M: 20[redacted]-[redacted] / -20	Y-M: 20[redacted]-[redacted] / -19
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	1 L	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 3	Y-M: 20[redacted]-[redacted] / 3
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	150 mL	OTHER: PER HOUR	Y-M: 20[redacted]-[redacted] / 3	Y-M: 20[redacted]-[redacted] / 4
MAGNESIUM SULFATE	2 g	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 3	Y-M: 20[redacted]-[redacted] / 3
CALCIUM CARBONATE	1250 mg	BID	Y-M: 20[redacted]-[redacted] / 4	Y-M: 20[redacted]-[redacted] / 9
SODIUM PHOSPHATE	15 mmol	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 4	Y-M: 20[redacted]-[redacted] / 4
TINZAPARIN	4500 IU	QD	Y-M: 20[redacted]-[redacted] / 4	Y-M: 20[redacted]-[redacted] / 9
VITAMIN D NOS	1000 IU	QD	Y-M: 20[redacted]-[redacted] / 4	Y-M: 20[redacted]-[redacted] / 9

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

Event Description	NOROVIRUS
Preferred term	ノロウイルス性胃腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 5
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 3): Creatine Kinase: 681 [0 - 195] U/L; NPTST080-C-REACTIVE PROTEIN: 78.6 [0 - 8] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 5): STOOL NPTST236-GASTROENTERITIS VIRUS PANEL: POSITIVE-NOROVIRUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 3): CHEST X-RAY: NO ABNORMALITIES; [redacted]20[redacted] (RX DAY 5): ECHOCARDIOGRAM: NO ABNORMALITIES

AE Stopped Rx Day	9
Duration of AE	5 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INTERCURRENT ILLNESS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はカナダの 2[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，ノロウイルス感染の事象を発現した。関連する病歴は，潰瘍性大腸炎，胆石性膵炎，原発性硬化性胆管炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与2日後＊　，被験者は下痢の増加（非重篤）を発症した。

投与3日後＊　，被験者はノロウイルス感染を発現した。投与9日後＊　，ノロウイルス感染は消失した。

投与3日後＊　，被験者は悪心，嘔吐及び脱水を発症し，救急科を受診した。　投与4日後＊，被験者は入院した。投与9日後＊　，被験者は退院した。

この間，被験者の母親及び父親も胃腸炎を発症した。

投与された薬剤は，ラクトリンゲルであった。

The patient's past medications include:

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Gastroenteritis norovirus (10068189) (Gastroenteritis norovirus (10068189)) [v.23.0] [10068189]

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 NOROVIRUS

- Investigator: INTERCURRENT ILLNESS

- AbbVie: Event is common in the general population. Norovirus is the most common viral cause of epidemic gastroenteritis worldwide; An additional risk factor includes family members with similar symptoms.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 78.6 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] CHEST X-RAY:** No abnormalities

[redacted] **20[redacted] CREATINE KINASE:** 681 U/L (normal 0 to 195)

[redacted] **20[redacted] ECHOCARDIOGRAM:** No abnormalities

[redacted] **20[redacted] GASTROENTERITIS VIRUS PANEL (STOOL):** Positive: Norovirus

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
アスパラギン酸アミノトランスフェラーゼ増加				X
血中クレアチンホスホキナーゼ増加				X
肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 45 mg	4[redacted]	MALE	ASIAN

Medical History	Onset Year
ARTHRALGIA	20[redacted]
BRONCHITIS	20[redacted]
CHRONIC GASTRITIS	20[redacted]
EMPHYSEMA	NOT REPORTED
EXTENSIVE UC/PANCOLITIS	20[redacted]
MILD ANEMIA	20[redacted]
NUMBNESS OF THE HANDS AND FEET	20[redacted]
PULMONARY INFLAMMATION	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: SPECIFY CT SCAN	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	30	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	40 mg	OTHER: QN	Y-M: 20[redacted]
METHYLPREDNISOLONE	50 mg	QD	Y-M: 20[redacted]
THALIDOMIDE	100 mg	OTHER: QN	Y-M: 20[redacted]
MESALAZINE	30 mL	OTHER: QN	Y-M: 20[redacted]
DEXAMETHASONE	2.5 mg	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg	QID	Y-M: 20[redacted]
MESALAZINE	60 mL	OTHER: QN	Y-M: 20[redacted]
DEXAMETHASONE	2.5 mg	QD	Y-M: 20[redacted]
THALIDOMIDE	50 mg	OTHER: QN	Y-M: 20[redacted]
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -353
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -313
MESALAZINE	30 mL	OTHER: QN	Y-M: 20[redacted] / -313
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -291
MESALAZINE	60 mL	OTHER: QN	Y-M: 20[redacted] / -291
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -264
ACETYLCYSTEINE	PRN g	PRN	Y-M: 20[redacted] / -278
MONTELUKAST	PRN mg	PRN	Y-M: 20[redacted] / -278
PROCATEROL	PRN ug	PRN	Y-M: 20[redacted] / -278
TIOTROPIUM	PRN OTHER: PRN	PRN	Y-M: 20[redacted] / -278
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -207
MESALAZINE	60 mL	OTHER: QN	Y-M: 20[redacted] / -181
METHYLPREDNISOLONE	40 mg	OTHER: QN	Y-M: 20[redacted] / -130
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -108
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -125
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	180 g	OTHER: ONCE	Y-M: 20[redacted] / -35
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -35
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / -14

ISONIAZID	0.3 g	QD	Y-M: 20[redacted] / -16
CALCIUM CARBONATE;COLECALCIFEROL	600 mg	QD	Y-M: 20[redacted] / -17
MIDAZOLAM	5 mg	QD	Y-M: 20[redacted] / -18
ALANINE;ARGININE;ASPARTIC ACID;CYSTEINE;GLUTAMIC ACID;GLYCEROL;GLYCINE;GLYCINE MAX;HISTIDINE;ISOLEUCINE;LECITHIN;LEUCINE;LYSINE;METHIONINE;PHENYLALANINE;PROLINE;SERINE;SODIUM BISULFITE;SORBITOL;THREO	250 mL	QD	Y-M: 20[redacted] / -20
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	1.5 g	TID	Y-M: 20[redacted] / -20
GLUCOSE	100 mL	QD	Y-M: 20[redacted] / -20
GLUCOSE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / -20
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	200 g	QD	Y-M: 20[redacted] / -20
MINERALS NOS	40 mL	QD	Y-M: 20[redacted] / -20
POTASSIUM	3 g	QD	Y-M: 20[redacted] / -20
PROPOFOL	APPROPRIATE OTHER: UNKNOWN	OTHER: ONCE	Y-M: 20[redacted] / -20
SODIUM CHLORIDE	10 mL	OTHER: ONCE	Y-M: 20[redacted] / -22
TUBERCULIN	50 IU	QD	Y-M: 20[redacted] / -22
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / -25
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -27

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
ACETYLCYSTEINE	PRN g	PRN	Y-M: 20[redacted] / -278	ONGOING
MONTELUKAST	PRN mg	PRN	Y-M: 20[redacted] / -278	ONGOING
PROCATEROL	PRN ug	PRN	Y-M: 20[redacted] / -278	ONGOING
TIOTROPIUM	PRN OTHER: PRN	PRN	Y-M: 20[redacted] / -278	ONGOING
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 16
CALCIUM CARBONATE;COLECALCIFEROL	600 mg	QD	Y-M: 20[redacted] / -17	Y-M: 20[redacted] / 56
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -27	Y-M: 20[redacted] / 56
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 23
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 30
METHYLPREDNISOLONE	14 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 35
METHYLPREDNISOLONE	12 mg	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 40

METHYLPREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 45
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 49
METHYLPREDNISOLONE	6 mg	QD	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 53
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 56
CAFFEINE;PARACETAMOL	0.5 g	QD	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 59
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / 59	ONGOING
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 59
MOXIFLOXACIN	0.4 g	QD	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 64
CALCIUM CARBONATE;COLECALCIFEROL	600 mg	PRN	Y-M: 20[redacted] / 60	ONGOING
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	120 g	OTHER: ONCE	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
OSELTAMIVIR	75 mg	BID	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 64
PROPOFOL	APPROPRIATE OTHER: UNKNOWN	OTHER: ONCE	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 61
AMINOPHYLLINE	0.25 g	QD	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
LEVOFLOXACIN	0.3 g	QD	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
SODIUM CHLORIDE	250 mL	QD	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
AMBROXOL	60 mg	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 65
CEFOTAXIME;SULBACTAM	3 g	OTHER: Q8H	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 74
GLUCOSE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 74
POTASSIUM PHOSPHATE DIBASIC;POTASSIUM PHOSPHATE MONOBASIC	2 mL	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 74
SODIUM CHLORIDE	10 mL	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 65
SODIUM CHLORIDE	100 mL	OTHER: Q8H	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 74
SODIUM CHLORIDE	100 mL	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 65
TUBERCULIN	50 IU	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 65

Event #1: Event of Interest - Hepatic Disorder

Event Description	AST INCREASED
Preferred term	アスパラギン酸アミノトランスフェラーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 43
Age at AE Onset	4[redacted]
Laboratory Testing	

NOT APPLICABLE

Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	61 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	19 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Event of Interest - Creatine Phosphokinase (CPK) Elevation

Event Description	CREATINE PHOSPHATE KINASE INCREASED
Preferred term	血中クレアチンホスホキナーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 43
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	61 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	19 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #3: Event of Interest - Creatine Phosphokinase (CPK) Elevation

Event Description	CREATINE KINASE ISOENZYME INCREASED
Preferred term	血中クレアチンホスホキナーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 43
Age at AE Onset	4[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Rx Day	65 (6 DAYS AFTER LAST TREATMENT)
Duration of AE	23 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	PULMONARY INFECTION
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 57
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 58): NPTST154-COVID-19 STATUS DETERMINATION: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 57): CHEST CT SCAN: NEW DIFFUSE GROUND-GLASS OPACITY IN BOTH LUNGS

AE Stopped Rx Day	63 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	7 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	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

[redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は中国の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，投与57日後＊　　に肺感染の事象を発現した。関連する病歴は，潰瘍性大腸炎，気管支炎，肺気腫，現喫煙者（1 日 1 箱を 30 年間）及び非飲酒者であった。

Event 4 の臨床経過：

投与57日後＊　，被験者は肺感染を発現した。投与63日後＊　，肺感染は消失した。

投与57日後＊　　，被験者は胸部 CT スキャン検査を受け，両肺に新たなびまん性すりガラス陰影が認められた。COVID-19 ウイルス検査（鼻咽頭）を実施し，結果は陰性であった。被験者は経口の抗炎症薬を投与された。

投与65日後＊　，被験者は息切れ，胸痛，並びに呼吸及び動作のより顕著な症状があり，入院した。別の COVID-19 検査を実施したが，これも陰性であった。結核菌検査（PPD）の結果は陰性であり，結核は考えられなかった。抗感染療法の後，症状は改善し，投与75日後＊　に被験者は退院した。

これらの事象により治験薬の投与は完全に中止された。

投与された薬剤は，モキシフロキサシン，オセルタミビルリン酸塩，アセチルシステイン，ブロムヘキシン塩酸塩，レボフロキサシン，アモキシシリンナトリウム・スルバクタムナトリウム合剤，デキサメタゾンリン酸エステルナトリウム，セフェピム塩酸塩水和物，セフォタキシムナトリウム・スルバクタム合剤，レボフロキサシン塩酸塩及びメトキシフェナミン化合物であった。

The patient's past medications include:

SOLU MEDROL for ULCERATIVE COLITIS ([redacted])

THALIDOMIDE for ULCERATIVE COLITIS ([redacted])

MEDROL for ULCERATIVE COLITIS ([redacted])

[redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

MESALAZINE ENEMAS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

DEXAMETHASONE SODIUM PHOSPHATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

Causality for UPADACITINIB (Blinded)

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1) Lung infection (10061229) (Pneumonia (10035664)) [v.23.0] [10061229]

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) Lung infection (10061229) (Pneumonia (10035664)) [v.23.0] [10061229]

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 PULMONARY INFECTION

- Investigator: Considered related to the study drugs

- AbbVie: Risk factors include pre-existing bronchitis, emphysema and on-going tobacco smoking (1 PPD for 30 years).

Event of PULMONARY INFECTION

- Investigator: Not applicable.

- AbbVie: Risk factors include pre-existing bronchitis, emphysema and on-going tobacco smoking (1 PPD for 30 years).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ALBUMIN:** 33.83 G/L (normal 40.00 to 55.00)

[redacted] **CHEST CT SCAN:** Abnormal - new diffuse ground-glass opacity in both lungs

[redacted] **CHEST CT SCAN:** Bilateral lungs scattered in ground glass like shadow; the overall change was little compared with before, considering the possibility of partial ventilation insufficiency or chronic inflammation. The area of the posterior segment of the upper lobe tip of the left lung and the anterior inner base segment of the lower lobe of the left lung was wider than before, except for the possibility of tuberculosis reburning, most of which were similar to before.

[redacted] **CHEST CT SCAN:** Calcified granulomas- absent, Pleural scarring- absent, Pleural thickening- absent, Signs of active TB- no, finding indicative of previous TB infection- yes. Inflammation of the middle lobe of the right lung with partial atelectasis is more advanced than before.

[redacted] **CHEST X-RAY:** Pulmonary infection.

[redacted] **CHEST X-RAY (SCREENING):** Normal

[redacted] **COVID-19 VIRUS TEST:** nasopharyngeal swab - negative

[redacted] **COVID-19 VIRUS TEST:** nasopharyngeal swab - negative

[redacted] **COVID-19 VIRUS TEST:** nasopharyngeal swab - negative

[redacted] **COVID-19 VIRUS TEST:** nasopharyngeal swab: Negative

[redacted] **HEMOGLOBIN:** 115.00 G/L (normal 120 to 160)

[redacted] **20[redacted] HEMOGLOBIN:** 112.0 G/L (normal 120 to 160)

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

[redacted] **20[redacted] PLATELET COUNT:** 359.0 X10**9/L (normal 100 to 300)

[redacted] **20[redacted] PLATELET COUNT:** 400 X10**9/L (normal 100 to 300)

[redacted] **20[redacted] PPD:** Negative

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Blood creatine phosphokinase increased: asymptomatic [redacted]20[redacted], etiology 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
筋膿瘍	X	X		X

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo	5[redacted]	MALE	WHITE

Medical History	Onset Year
DIABETES MELLITUS	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
OBSTRUCTIVE SLEEP APNEA	20[redacted]
PERFORATION OF A DUODENAL ULCER	20[redacted]
SIDEROPENIC ANEMIA	20[redacted]
STATUS POST SEPTOPLASTY	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: SEPTOPLASTY	20[redacted]
PRIOR PROCEDURES: SURGICAL TREATMENT OF PERFORATED DUODENAL ULCER	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	UNKNOWN			
CIGARETTES	FORMER	2 PACK	33	20[redacted]
CIGARS	UNKNOWN			
E-CIGARETTES	UNKNOWN			
PIPES	UNKNOWN			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	150 mg	BID	Y-M: 20[redacted] / -323
MESALAZINE	500 mg	OTHER: 3*2 PILLS DAILY	Y-M: 20[redacted] / -293
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -271
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -64
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACKAGE	BID	Y-M: 20[redacted] / -15
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / -7
AMLODIPINE;PERINDOPRIL	5/10 mg	QD	Y: 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
MESALAZINE	500 mg	OTHER: 3*2 PILLS DAILY	Y-M: 20[redacted] / -293	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -271	ONGOING
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / -7	ONGOING
VILDAGLIPTIN	50 mg	QD	Y-M: 20[redacted] / 20	ONGOING
IBUPROFEN	600 mg	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 49
IBUPROFEN	600 mg	BID	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 52
AMOXICILLIN;CLAVULANIC ACID	1 g	BID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 62
PROPOFOL	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
SUFENTANIL	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
AMLODIPINE;PERINDOPRIL	5/10 mg	QD	Y: 20[redacted]	ONGOING

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

Event Description	GLUTEAL ABSCESS
Preferred term	筋膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 47
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 52): ABDOMEN AND PELVIS CT SCAN WITH IV CONTRAST: ISCHIORECTAL ABSCESS	
AE Stopped Rx Day	91 (33 DAYS AFTER LAST TREATMENT)
Duration of AE	45 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DISEASE PROGRESSION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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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
胞隔炎		X		
貧血	X			X
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo /P2:ABT-494 45 mg	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA DUE TO ULCERATIVE COLLITIS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
ULCER. COLITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo			[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 70	14

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DROSPIRENONE;ETHINYLESTRADIOL	3 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
CALCIUM CARBONATE	400 mg	QD	Y-M: 20[redacted]
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
FLUCONAZOLE	200.000 mg	QD	Y-M: 20[redacted]
FLUCONAZOLE	400.000 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
BROMAZEPAM	3 mg	PRN	Y-M: 20[redacted] / -325
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -325
PROPOFOL	2,5 mg	QD	Y-M: 20[redacted] / -28
CITRIC ACID;MACROGOL 4000;POTASSIUM;SIMETICONE;SODIUM CHLORIDE;SODIUM CITRATE;SODIUM SULFATE	4000 mL	QD	Y-M: 20[redacted] / -29
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -37
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -37
AZATHIOPRINE	50 mg	BID	Y: 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
DROSPIRENONE;ETHINYLESTRADIOL	3 mg	QD	Y-M: 20[redacted]	ONGOING
CALCIUM CARBONATE	400 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 83
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 83
BROMAZEPAM	3 mg	PRN	Y-M: 20[redacted] / -325	Y-M: 20[redacted] / 83
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -37	Y-M: 20[redacted] / 63
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -37	Y-M: 20[redacted] / 63
CITRIC ACID;MACROGOL 4000;POTASSIUM;SIMETICONE;SODIUM CHLORIDE;SODIUM CITRATE;SODIUM SULFATE	4000 mL	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
DIAZEPAM	10 mg	OTHER: SINGLE	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57

		DOSE		
IRON	10 mL	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
SODIUM CHLORIDE	100 mL	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
IRON	100 mg	QD	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 69
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 70
POTASSIUM	1 g	QD	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 83
BLOOD AND RELATED PRODUCTS	300 ONE DOSE mL	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 68
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 83
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 71
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 83
VENLAFAXINE	75 mg	QD	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 83
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 83
LIDOCAINE	1 OTHER: ONE SPRAY IN THE MOUTH	PRN	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 82
TETRACAINE	1 OTHER: ONE SPRAY IN THE MOUTH	PRN	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 82
HYDROCORTISONE	100 mg	QD	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 84
HYDROCORTISONE	50 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 86
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 90	Y-M: 20[redacted] / 96
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 90	ONGOING

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

Event Description	WORSENING OF ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 57
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 64): Hemoglobin: 78 [120 - 160] G/L; [redacted]20[redacted] (RX DAY 68): Hemoglobin: 116 [120 - 160] G/L

Microbiology

[redacted]20[redacted] (RX DAY 65): OTHER NASAL SWAB NPTST152-COVID 19: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 64): ULTRASOUNDOF HEART: NORMAL; [redacted]20[redacted] (RX DAY 70): HRCT LUNGS: ABNORMAL FINDINGS

AE Stopped Rx Day 70

Duration of AE	14 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HIGH ACTIVITY UC AND GIT BLEEDING. PATIENT WAS PLANNED ADMITTED TO HOSPITAL SCHEDULED FOR CORRECTION FOR LOW HEMOGLOBIN, HOSPITALIZATION WAS PROVIDED FOR THE PATIENT DUE TO DIFFICULTIES IN TRANSPORTI
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	RELAPS UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 57
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 83): Erythrocytes: 3.47 [3.39 - 4.03] 10^12/L; Hemoglobin: 88 [87 - 106] G/L; Leukocytes: 16.3 [7.99 - 16.3] 10^9/L; NPTST080-C-REACTIVE PROTEIN: 38.9 [32.6 - 38.9] MG/L; [redacted]20[redacted] (RX DAY 90): Erythrocytes: 4.03 [3.39 - 4.03] 10^12/L; Hemoglobin: 106 [87 - 106] G/L; Leukocytes: 7.99 [7.99 - 16.3] 10^9/L; NPTST077-C REACTIVE PROTEIN: 33.0 [32.6 - 38.9] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 84): LAPAROSCOPY SUBTOTAL COLECTOMIA: SURGERY WITHOUT COMPLICATION. CORTICOSTEROID THERATPY WAS TERMINATED. SUBTOTAL COLECTOMY+TERMINAL ILEOSTOM

AE Stopped Rx Day	90 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	34 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #3: AE Leading to Discontinuation of Study Drug

Event Description	ALVEOLITIS
Preferred term	胞隔炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 70
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	90 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	21 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はチェコ共和国の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及びウパダシチニブが投与され，潰瘍性大腸炎の再燃及び貧血の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，潰瘍性大腸炎による貧血，非喫煙者及び非飲酒者であった。

Event 1 及び 2 の臨床経過：

投与57日後＊　　，被験者は潰瘍性大腸炎の再燃及び貧血の悪化を発現した。　　投与70日後＊，貧血の悪化は消失した。投与90日後＊　　，潰瘍性大腸炎の再燃は消失した。

投与64日後＊　　，被験者は，病歴にある潰瘍性大腸炎に伴う貧血を，各来院時でも発現していると診断され，入院した。入院はヘモグロビンの低値を是正するために計画された。輸血が計画された。徴候や症状はなく，臨床検査値としてヘモグロビン値が低いのみであった。治験責任医師の判断によると，ヘモグロビン値低下の原因は，潰瘍性大腸炎に関連した消化管出血と考えられた。投与70日後＊　　，被験者は退院した。

投与70日後＊　，胞隔炎（非重篤）により，治験薬の投与は中止された。

投与83日後＊　，被験者は潰瘍性大腸炎関連の症状で再入院した。被験者には息切れ，咳嗽及び貧血の症状があった。被験者は腹部超音波検査及び CT スキャン検査を受けた。投与83日後＊　，被験者は腹腔鏡下の結腸亜全摘術及び末端回腸瘻造設を受けた。被験者は合併症を発現しなかった。投与90日後＊　，被験者は退院した。

投与された薬剤及び処置は，メドロール，ciplox，輸血，entizol，生理食塩水，olimel 及びフェインジェクトであった。

The patient's past medications include:

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

AZATHIOPRIN for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

MEDROL for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Ulcerative colitis relapse (10082448)　(Colitis ulcerative (10009900))　[v.23.0]　[10082448]

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

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

Dechallenge: Not Applicable

2)　Anemia aggravated (10054309)　(Anaemia (10002034))　[v.23.0]　[10054309]

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

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

Dechallenge: Not Applicable

Causality for UPADACITINIB (Open Label)

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1) Ulcerative colitis relapse (10082448) (Colitis ulcerative (10009900)) [v.23.0] [10082448]

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

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

Dechallenge: Not Applicable

2) Anemia aggravated (10054309) (Anaemia (10002034)) [v.23.0] [10054309]

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 RELAPSE UC

- Investigator: Ulcerative colitis

- AbbVie: Event more likely related to complication from pre-existing Ulcerative colitis.

Event of WORSENING OF ANEMIA

- Investigator: Patient was planned admitted to hospital scheduled for correction for low hemoglobin. Hospitalization was provided for the patient due to difficulties in transporting to the site.

- AbbVie: Event more likely related to pre-existing Ulcerative colitis and anemia.

Alternative Etiology for UPADACITINIB (Open Label)

Event of RELAPSE UC

- Investigator: Ulcerative colitis

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

Event of WORSENING OF ANEMIA

- Investigator: Patient was planned admitted to hospital scheduled for correction for low hemoglobin. Hospitalization was provided for the patient due to difficulties in transporting to the site.

- AbbVie: Event more likely related to pre-existing Ulcerative colitis and anemia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] C REATIVE PROTEIN:** 33.0 mg/l (normal 32.6 to 38.9)

[redacted] **20[redacted] COLONOSCOPY**: A clear demarcation between normal and inflamed colonic mucosa was seen. The distance of demarcation from the anal verge was 60 cm.

[redacted] **20[redacted] COVID 19 TEST:** negative

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 38.9 MG/L (normal 32.6 to 38.9)

[redacted] **20[redacted] HEMOGLOBIN:** 65 G/L (normal 120 to 160)

[redacted] **20[redacted] HEMOGLOBIN:** 78 G/L (normal 120 to 160)

[redacted] **20[redacted] HEMOGLOBIN:** 88 G/L (normal 87 to 106)

[redacted] **20[redacted] HEMOGLOBIN:** 106 G/L (normal 87 to 106)

[redacted] **20[redacted] HGB:** 116 G/L (normal 120 to 160)

[redacted] **20[redacted] HIGH-RESOLUTION COMPUTERIZED TOMOGRAPHY OF LUNG:** abnormal findings

[redacted] **20[redacted] RBC:** 4.03 X10**12/L (normal 3.39 to 4.03)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.47 X10**12/L (normal 3.39 to 4.03)

[redacted] **20[redacted] ULTRASOUND OF HEART:** normal

[redacted] **20[redacted] WBC:** 7.99 X10**9/L (normal 7.99 to 13.6)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 16.3 X10**9/L (normal 7.99 to 16.3)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Anaemia: described as worsening of anemia.

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo	2[redacted]	MALE	WHITE

Medical History	Onset Year
LEFT SIDED UC	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo			[redacted]20[redacted] / 1	[redacted]20[redacted] / 15	15

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	3200 mg	QD	Y-M: 20[redacted] / -337
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -337
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -219

BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -247
MESALAZINE	1 g	QD	Y-M: 20[redacted] / -247
MESALAZINE	4000 mg	QD	Y-M: 20[redacted] / -247
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -44
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19[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
MESALAZINE	4000 mg	QD	Y-M: 20[redacted] / -247	ONGOING
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -44	ONGOING
INFLIXIMAB	400 mg	OTHER: 0,2 ND 4 WEEK STARTING PERIOD	Y-M: 20[redacted] / 19	ONGOING

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

Event Description	UC WORSENING
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 12
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はフィンランドの 2[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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与12日後＊　　，被験者は潰瘍性大腸炎の悪化を発現した。

被験者は脱力及び下痢を経験し，生活の質が制限された。被験者は病気で仕事を休まなければならなかった。

本事象により治験薬の投与は完全に中止された。

投与された薬剤はレミケードであった。

The patient's past medications include:

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

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

Causality for UPADACITINIB (Blinded)

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1)　UC aggravated (10045283)　(Colitis ulcerative (10009900))　[v.22.1]　[10045283]

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 UC WORSENING

- Investigator: Not applicable

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

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 45 mg	3[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
PRIMARY SCLEROSING CHOLANGITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 8	8

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]-[redacted]

NOT CODED	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
MESALAZINE	2 g	QD	Y-M: 20[redacted]
MESALAZINE	800 mg	QID	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	2 mg/kg	QD	Y-M: 20[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	50 mg	QD	Y-M: 20[redacted]
USTEKINUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	NOT REPORTED	QD	Y-M: 20[redacted]
URSODEOXYCHOLIC ACID	1000 mg	QD	Y-M: 20[redacted]
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	2 OTHER: BAG	QD	Y-M: 20[redacted] / -10

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	2 g	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	800 mg	QID	Y-M: 20[redacted]	Not reported
URSODEOXYCHOLIC ACID	1000 mg	QD	Y-M: 20[redacted]	ONGOING
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	2 OTHER: BAG	QD	Y-M: 20[redacted] / -10	Y-M: 20[redacted] / -10
ENOXAPARIN	4000 IU	QD	Y-M: 20[redacted] / 15	ONGOING
GENERAL NUTRIENTS	2 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 16	ONGOING
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 27
CICLOSPORIN	150 mg	QD	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 27
CICLOSPORIN	150 mg	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 30
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 32
TOFACITINIB	10 mg	BID	Y-M: 20[redacted] / 31	ONGOING
PREDNISOLONE	50 mg	QD	Y-M: 20[redacted] / 33	ONGOING
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 15

Event #1: AE Leading to Discontinuation of Study Drug

Event Description	FLARE UP OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 8
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	15 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	SEVERE FLARE UP OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 15 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 15): Albumin: 32 [35 - 52] G/L; Hemoglobin: 134 [130 - 170] G/L; NPTST159-CRP: 10 [NOT REPORTED - 6] mg/L; [redacted]20[redacted] (RX DAY 22): NPTST118-CLOSTRIDIUM DIFFICILE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST470-STOOL CULTURE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 33): Albumin: 31 [35 - 52] G/L; Hemoglobin: 142 [130 - 170] G/L; NPTST159-CRP: 3 [NOT REPORTED - 6] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 104): COLONOSCOPY: COLONOSCOPIC CONTROL CONFIRMS PERSISTENCE OF ACTIVE DISEASE

AE Stopped Rx Day	146 (138 DAYS AFTER LAST TREATMENT)
Duration of AE	132 DAYS
Severity	SEVERE

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はフランスの 3[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，潰瘍性大腸炎の重度の再燃の事象を発現した。関連する病歴は，潰瘍性大腸炎，原発性硬化性胆管炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与15日後＊　，被験者は潰瘍性大腸炎の重度の再燃を発現した。投与146日後＊　，潰瘍性大腸炎の重度の再燃は消失した。

本事象の発現前，被験者は投与8日後＊　に潰瘍性大腸炎の再発（非重篤）を発現し始めた。この非重篤な事象により治験薬の投与は完全に中止され，被験者は本治験への参加を中止した。

投与15日後＊　，潰瘍性大腸炎の再燃は重症化し，経口コルチコステロイドに抵抗性を示したため，被験者は入院した。被験者は腹痛，無力症，直腸出血及び 1 日 12 回の排便を発現していた。被験者は solupred（60 mg）の静脈内投与を受けた。被験者はステロイドが効かず，次にシクロスポリンで治療したが，これも効かなかった。投与31日後＊　，被験者はトファシチニブを開始した。高用量（10 mg を 1 日 2 回）にもかかわらず，トファシチニブの治療は効果が認められなかった。投与33日後＊　，被験者は退院した。

投与104日後＊　，結腸内視鏡検査で活動性疾患の持続が確認された。投与146日後＊　，回腸瘻造設により保護された回腸肛門吻合を伴う結腸直腸全摘術が行われた。

投与された薬剤は，solupred，メチルプレドニゾロン，lovenox，delical boisson fruitee，トファシチニブ，シクロスポリン及びネオーラルであった。

The patient's past medications include:

IMUREL for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

SOLUPRED for ULCERATIVE COLITIS ([redacted])

USTEKINUMAB for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.23.0] [10009901]

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 SEVERE FLARE UP OF ULCERATIVE COLITIS

- Investigator: ULCERATIVE COLITIS

- AbbVie: Reported event more likely related to pre-existing Ulcerative Colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20**[redacted] **ALBUMIN:** 32 G/L (normal 35 to 52)

[redacted] **20**[redacted] **ALBUMIN:** 31 G/L (normal 35 to 52)

[redacted] **20**[redacted] **C DIFFICILE:** negative

[redacted] **20**[redacted] **CRP:** 10 MG/L (normal 0 to 6)

[redacted] **20**[redacted] **CRP:** 3 mb/l (normal <6)

[redacted] **20**[redacted] **HEMOGLOBIN:** 13.4 G/DL (normal 13 to 17)

[redacted] **20**[redacted] **HEMOGLOBIN:** 14.2 G/DL (normal 13 to 17)

[redacted] **20**[redacted] **STOOL 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
潰瘍性大腸炎	X	X		
ヘモグロビン減少		X		X

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
ABDOMINAL PAIN	20[redacted]
ASTHENIA	20[redacted]
DIARHEA	20[redacted]
LEFT SIDED UC	20[redacted]
RECTAL BLEEDING	20[redacted]
THROMBOCYTOSIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo			[redacted]20[redacted] / 1	[redacted]20[redacted] / 3	3

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / -12
ENOXAPARIN	0.4 mL	QD	Y-M: 20[redacted] / -7
PHOSPHORIC ACID;SODIUM PHOSPHATE	30 OTHER: TABLETS	QD	Y-M: 20[redacted] / -9

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Not reported	Not reported
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Not reported	Not reported
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Not reported	Not reported
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Not reported	Not reported
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]	Not reported
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / -12	Y-M: 20[redacted] / 7
ENOXAPARIN	0.4 mL	QD	Y-M: 20[redacted] / -7	ONGOING
PHOSPHORIC ACID;SODIUM PHOSPHATE	30 OTHER: TABLETS	QD	Y-M: 20[redacted] / -9	Y-M: 20[redacted] / -9
CICLOSPORIN	2 mg/kg	QD	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 16
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 21
SULFAMETHOXAZOLE;TRIMETHOPRIM	800/160 mg	OTHER: 3 TIMES PER WEEK	Y-M: 20[redacted] / 14	ONGOING
CICLOSPORIN	50 mg	BID	Y-M: 20[redacted] / 17	ONGOING
PREDNISOLONE	50 mg	QD	Y-M: 20[redacted] / 18	ONGOING
TRAMADOL	50 mg	QID	Y-M: 20[redacted] / 9	ONGOING

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

Event Description	UC FLARE DISEASE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 3
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug, Event of Interest - Anemia

Event Description	LOW HEMOGLOBIN LEVEL
Preferred term	ヘモグロビン減少
AE Onset Date / Rx Day	[redacted]20[redacted] / 17 (14 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:36
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はフランスの 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，潰瘍性大腸炎の再燃の事象を発現した。関連する病歴は，直腸出血，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与3日後＊　　，被験者は潰瘍性大腸炎の再燃を発現した。

投与3日後＊　　，被験者は潰瘍性大腸炎の再燃のため入院した。被験者は非常に衰弱しており，便に多くの血が混じった激しい下痢が見られた。投与17日後＊　　，被験者は体調が改善し，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。

投与された薬剤は，トラマドール，solupred 及びシクロスポリンであった。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS (Started [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS

REMICADE for ULCERATIVE COLITIS

VEDOLIZUMAB for ULCERATIVE COLITIS

IMUREL for ULCERATIVE COLITIS

Causality for UPADACITINIB (Blinded)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.23.0]　[10009901]

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

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

Dechallenge: Yes

Alternative Etiology for UPADACITINIB (Blinded)

Event of UC FLARE DISEASE

- Investigator: Not applicable.

- AbbVie: Event more likely related to pre-existing Ulcerative Colitis.

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 45 mg /P2:ABT-494 45 mg	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 113	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	3 g	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	80 mg	QD	Y-M: 20[redacted]
VITAMIN D NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]
BUDESONIDE	1 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -186
MIDAZOLAM	5 mg	QD	Y-M: 20[redacted] / -27
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19[redacted]
AZATHIOPRINE	50 mg	QD	Y: 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
MESALAZINE	3 g	QD	Y-M: 20[redacted]	ONGOING
VITAMIN D NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]	ONGOING
ASCORBIC ACID;IRON;NICOTINAMIDE;RIBOFLAVIN; THIAMINE	62.5 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
CALCIUM;POTASSIUM;SODIUM	500 mL	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
CIPROFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 58
GLUCOSE	500 mL	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
METRONIDAZOLE	500 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 58
MIDAZOLAM	5 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
PETHIDINE	50 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
SODIUM CHLORIDE	100 mL	QD	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 58
MIDAZOLAM	5 mg	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 114
PETHIDINE	50 mg	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 114

Event #1: Event of Interest - Anemia

Event Description	ANAEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 29
Age at AE Onset	2[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	HYPOTENSION
Preferred term	低血圧
AE Onset Date / Rx Day	[redacted]20[redacted] / 57
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 57): Hematocrit: 0.28 [0.34 - 0.45] FRACTION OF 1; Hemoglobin: 85 [120 - 150] G/L; Leukocytes: 14.99 [4 - 10] 10^9/L; NPTST296-INR: 1.28 [0.85 - 1.25] INR; Platelets: 445 [150 - 400] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 57): ABDOMINAL X-RAY: NEGATIVE

AE Stopped Rx Day	58
Duration of AE	2 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ANAMEIA AND COLONOSCOPY PREPARATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

[redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はハンガリーの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，低血圧の事象を発現した。関連する病歴は，潰瘍性大腸炎（広範囲な潰瘍性大腸炎/全大腸炎型），非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与57日後＊　，被験者は低血圧を発現した。投与58日後＊　，低血圧は消失した。

被験者は 投与29日後＊　に貧血（非重篤）を発現しており，本事象は未だ継続中と考えられていた。

投与57日後＊　，被験者は入院した。被験者は結腸内視鏡検査を受けた。その後，被験者は低血圧及び虚脱前の状態を経験した。被験者は薬物療法を受け，リンゲル液を注入された。被験者の血圧は安定し，退院時には回復した状態であった。投与58日後＊　，被験者は退院した。本報告時点で，入院中の詳細な情報は得られていなかった。

投与された薬剤は，ブドウ糖，リンゲル液，ferrlecit，salsol，klion 及び cifran であった。

The patient's past medications include:

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

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

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

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

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

Causality for ABT-494 (Blinded)

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1)　Hypotension (10021097)　(Hypotension (10021097))　[v.22.0]　[10021097]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of HYPOTENSION

- Investigator: Not reported

- AbbVie: event is more likely related to recent colonoscopy procedure.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL X-RAY:** Negative

[redacted] **20[redacted] BLOOD PRESSURE:** 120/70- mmHg (screening)

[redacted] **20[redacted] BLOOD PRESSURE:** 130/80- mmHg (screening)

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

[redacted] **20[redacted] COLONOSCOPY:** No normal mucosa (pancolitis). Central Reader Endoscopy Subscore = 3

[redacted] **20[redacted] HEMATOCRIT:** 0.28 Ratio (normal 0.34 to 0.45)

[redacted] **20[redacted] HEMOGLOBIN:** 85 G/L (normal 120 to 150)

[redacted] **20[redacted] INR:** 1.28 No Unit (normal 0.85 to 1.25)

[redacted] **20[redacted] PLATELET COUNT:** 445 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 14.99 X10**9/L (norm al 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
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 45 mg /P2:ABT-494 45 mg	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
PERIPHERAL ARTHROPATHY	20[redacted]
SACRO-COCCYGEAL FISTULA	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 59	[redacted]20[redacted] / 99	41

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
GOLIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -306
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -257
MESALAZINE	3600 mg	QD	Y-M: 20[redacted] / -155
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -148
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -106
COLECALCIFEROL	25000 OTHER: U	OTHER: EVERY 15 DAYS	Y-M: 20[redacted] / -71
PREDNISONE	37.5 mg	QD	Y-M: 20[redacted] / -78

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	3600 mg	QD	Y-M: 20[redacted] / -155	Y-M: 20[redacted] / 61
COLECALCIFEROL	25000 OTHER: U	OTHER: EVERY 15 DAYS	Y-M: 20[redacted] / -71	ONGOING
ENEMAS	100 mL	BID	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
CIPROFLOXACIN	250 mg	TID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 70
CORTICOSTEROIDS	1 mg/kg	QD	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 69
MESALAZINE	2400 mg	BID	Y-M: 20[redacted] / 61	ONGOING
METRONIDAZOLE	250 mg	TID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 74

Event #1: Serious Adverse Event

Event Description	DISEASE WORSENING ULCERATIVE COLITIS DISEASE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 61
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 61): Hematocrit: 0.42 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 137 [120 - 160] G/L; Leukocytes: 6.6 [4 - 10] 10^9/L; NPTST159-CRP: 1.44 [0 - 0.5] MG/DL; NPTST323-MCV: 96.3 [76 - 96] FL; Nitrite: 14 [17 - 45] %; Platelets: 253 [150 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 68): Hematocrit: 0.41 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 133 [120 - 160] G/L; Leukocytes: 12.2 [4 - 10] 10^9/L; NPTST159-CRP: 0.1 [0 - 0.5] MG/DL; NPTST323-MCV: 96.8 [79 - 96] FL; Nitrite: 10 [17 - 45] %; Platelets: 258 [150 - 400] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 64): ABDOMINAL X-RAY: MORPHOLOGICAL ALTERATION OF THE LEFT COLON, COMPATIBLE WITH INFLAMMATION. MODERATE METEORIC DISTENSION OF INTESTINAL TRACTS

(SMALL AND PART OF COLON). NO SIGNIFICANT HYDRO-AERIAL LEVELS. NO IMAGES OF FREE INTRAPERITONEAL GAS.

AE Stopped Rx Day	70
Duration of AE	10 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NONE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はイタリアの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，仙骨―尾骨間の瘻孔，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与61日後＊　　，潰瘍性大腸炎の悪化を発現した。投与70日後＊　　，潰瘍性大腸炎の悪化は消失した。

投与61日後＊　　，被験者は疾患が悪化し，入院した。関連する徴候及び症状は，発熱，悪心及び腹痛であった。症状は内科的治療で改善した。投与70日後＊　　，被験者は退院した。

投与された薬剤は，mesavacol，フラジール，シプロフロキサシン及び deltacortene であった。

The patient's past medications include:

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

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

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

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

DELTACORTENE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.22.1] [10009901]

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 DISEASE WORSENING ULCERATIVE COLITIS DISEASE

- Investigator: None

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL X-RAY:** Morphological alteration of the left colon, compatible with inflammation. Moderate meteoric distension of intestinal tracts (small and part of colon). No significant hydro-aerial levels. No images of free intraperitoneal gas.

[redacted] **COLONOSCOPY:** Not reported

[redacted] **CRP:** 1.44 mg/dL (normal 0 to 0.6)

[redacted] **CRP:** 0.05 mg/dL (normal 0 to 0.6)

[redacted] **HB:** 13.6 No units

[redacted] **20[redacted] HEMATOCRIT:** 42 % (normal 35 to 47)

[redacted] **20[redacted] HEMATOCRIT:** 41.2 % (normal 35 to 47)

[redacted] **20[redacted] HEMOGLOBIN:** 13.7 G/DL (normal 12 to 16)

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

[redacted] **20[redacted] MCV:** 96.3 FL (normal 76 to 96)

[redacted] **20[redacted] MCV:** 96.8 FL (normal 79 to 96)

[redacted] **20[redacted] NITRITE:** 14 mg% (Normal 17-45)

[redacted] **20[redacted] NITRITE:** 10 mg% (Normal 17-45)

[redacted] **20[redacted] PLATELET COUNT:** 253 X10**3/MCL (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT:** 258 X10**3/MCL (normal 150 to 400)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 6.60 X10**3/MCL (normal 4 to 10)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 12.20 X10**3/MCL (normal 4 to 10)

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
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo	3[redacted]	MALE	WHITE

Medical History	Onset Year
ACNE	20[redacted]
LEFT SIDED UC	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]-[redacted]

MESALAZINE	800 mg	TID	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
GOLIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
CODEINE;PARACETAMOL	500/30 OTHER: MG/MG	OTHER: AS NEEDED	Y-M: 20[redacted] / -188
PREDNISONE	50 mg	QD	Y-M: 20[redacted] / -188
PROPOFOL	215 mg	OTHER: ONCE	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 / Stop Year-Month / RX Day	
CODEINE;PARACETAMOL	500/30 OTHER: MG/MG	OTHER: AS NEEDED	Y-M: 20[redacted] / -188	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 3	ONGOING
MIDAZOLAM	2.5 mg	OTHER: JUST ONCE	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 59
PETHIDINE	50 mg	OTHER: JUST ONCE	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 59
SOLUTIONS FOR PARENTERAL NUTRITION	2000 mL	QD	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 71
ALPRAZOLAM	10 gtt	TID	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 73
IRON	20 mL	OTHER: ONCE	Y-M: 20[redacted] / 73	Y-M: 20[redacted] / 73

Event #1: Serious Adverse Event

Event Description	WORSERING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 64 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 64): Hematocrit: 0.32 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 108 [140 - 180] G/L; NPTST080-C-REACTIVE PROTEIN: 122.58 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 65): Hematocrit: 0.33 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 109 [140 - 180] G/L; [redacted]20[redacted] (RX DAY 66): Eosinophils: 0.6 [0 - 0.45] 10^9/L; Hematocrit: 0.33 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 108 [140 - 180] G/L; NPTST080-C-REACTIVE PROTEIN: 87.89 [0 - 5] MG/L; NPTST297-IRON: 4.1 [11.64 - 31.33] UMOL/L; [redacted]20[redacted] (RX DAY 67): NPTST510-UREA: 1.8 [2.9 - 8.2] MMOL/L; NPTST510-UREA: 39.62 [141 - 494] MMOL/L; [redacted]20[redacted] (RX DAY 68): Eosinophils: 0.6 [0 - 0.45] 10^9/L; Hematocrit: 0.33 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 108 [140 - 180] G/L; NPTST080-C-REACTIVE PROTEIN: 20.82 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 71): Hematocrit: 0.35 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 116 [140 - 180] G/L; NPTST510-UREA: 2.4 [2.9 - 8.2] MMOL/L; NPTST510-UREA: 74.24 [141 - 494]

MMOL/L; [redacted] (RX DAY 72): NPTST510-UREA: 104.8 [141 - 494] MMOL/L; [redacted] (RX DAY 73): Eosinophils: 0.6 [0 - 0.45] 10^9/L; Hematocrit: 0.34 [0.42 - 0.52] FRACTION OF 1; Hemoglobin: 110 [140 - 180] G/L

Microbiology

[redacted] (RX DAY 65): BLOOD NPTST035-ANTIGENE ADENOVITRUS RESEARCH R: NEGATIVE; BLOOD NPTST036-ANTIGENE ROTAVIRUS RESEARCH RAP: NEGATIVE; STOOL NPTST118-CLOSTRIDIUM DIFFICILE: NEGATIVE; STOOL NPTST149-COPROPARASSITOLOGICAL EXAMINATI: NEGATIVE; STOOL NPTST532-YERSINIA RESEARCH: NEGATIVE; [redacted] (RX DAY 66): OTHER PLASMA NPTST113-CITOMEGALOVIRUS SEQUENCES DNA R: NEGATIVE; [redacted] (RX DAY 67): STOOL NPTST149-COPROPARASSITOLOGICAL EXAMINATI: NEGATIVE-SOME WHITE BLOOD CELLS AND SEVERAL BLASTOSPORES; STOOL NPTST149-COPROPARASSITOLOGICAL EXAMINATI: NEGATIVE-SEVERAL WHITE BLOOD CELLS; [redacted] (RX DAY 73): OTHER SIGMA (A) AND RECTUM (B) BIOPSIES NPTST270-HISTOLOGICAL EXAMINATION: POSITIVE-MUCOUS MEMBRANE OF THE LARGE INTESTINE WITH ARCHITECTURAL DISTORTION AND WITH CHRONIC ACTIVE INFLAMMATION WITH AN ULCERATIVE FOOTPRINT (A), WITH CHRONIC ACTIVE EROSIVE PHLOGOSIS (B).

SAE Supplemental Procedure

[redacted] (RX DAY 65): CHEST RADIOGRAPHY: NORMAL; PLAIN ABDOMINAL RADIOGRAPHY: NORMAL; [redacted] (RX DAY 67): ECG: NORMAL; [redacted] (RX DAY 69): COMPLETE ABDOMEN ECOGRAPHY: THERE IS EVIDENCE OF THICKENING OF THE WALLS OF THE DESCENDANT AND OF THE SIGMA WITH MODEST HYPEREMIA AT DOPPLER, TO BE COMPARED TO INFLAMMATORY PHENOMENA (KNOWN PICTURE OF ULCERATIVE RECTOCOLITIS).; [redacted] (RX DAY 71): PSYCHIATRIC VISIT: NEGATIVE PSYCHIATRIC HISTORY. FROM THE PSYCHIC EXAMINATION, NO DISTURBANCES IN THE FORM OR CONTENT OF THOUGHT EMERGE. NO DISTURBANCES REPORTED PERCEPTIONS. COMPLAINS IN THE LAST 3-4 DAYS AN INCREASI NG ANXIOUS STATE REACTIVE TO THE PROLONGED STAY AND TO THE CONSEQUENCES OF THE DISEASE ON FAMILY AND WORKING LIFE. DENIES SELF-INJURIOUS INTENTIONALITY. HERE I'M OCCASIONAL INITIAL INSOMNIA. ALREAD Y REQUESTING PSYCHOLOGICAL TREATMENT COUNCIL. - ALPRAZOLAM GTT, 10 HOURS IN THE MORNING, 10 DAYS AFTER LUNCH AND 10 DAYS AT 20:00; PSYCOLOGICAL VISIT: FIRST PSYCHOLOGICAL VISIT. A REACTIVE CURRENT DISTRESS EMERGES HEALTH SITUATION. HE DESCRIBES HIMSELF AS A PERSON USED TO PLAN ONE'S LIFE IN DETAIL AND A CURRENT PERCEPTION OF PARTIAL LOSS OF CONTRO L EMERGES (FOR THE NEED TO ENTRUST THEIR CARE TO OTHERS). COMPARED TO THE INTERVENTION IT APPEARS TO BE IN AGREEMENT AND MOTIVATED TO THE SAME BUT REPORTS THAT IT IS NOT NOW FOCUSED ON IT. WE AGREE PSYCHOLOGICAL SUPPORT INTERVIEWS AIMED AT ENCOURAGING A PSYCHOLOGICAL ADAPTATION TO CURRENT SITUATION.; [redacted] (RX DAY 73): RECTOSIGMOIDOSCOPY: ACTIVE ULCERATIVE COLITIS GRADE SEVERE

AE Stopped Rx Day	87 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	24 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	EXACERBATION OF THE DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 80 (22 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 80): Leukocytes: 18 [5.2 - 12.4] 10^9/L; NPTST159-CRP: 39 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 80): COLECTOMY WITH ILEOSTOMY: THE PATIENT WAS DISCHARGED WITH WELLBEING; [redacted]20[redacted] (RX DAY 81): ABDOMINAL CT SCAN: BOWEL DISTENSION, NO PERFORATION

AE Stopped Rx Day	87 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PROGRESSION OF DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はイタリアの 3[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，投与64日後＊　　及び 投与80日後＊　に潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 及び 2 の臨床経過：

投与64日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与80日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与87日後＊　，潰瘍性大腸炎の悪化は消失した。

本事象の発現前，投与59日後＊　に被験者は潰瘍性大腸炎の悪化（非重篤）を発現しており，治験薬の投与は完全に中止された。

投与64日後＊　，被験者は数回の下痢及び腹痛を呈し，救急治療室を受診した。被験者はさらなる検査のため入院した。感染症の存在は認められなかった。被験者には非経口栄養が投与され，症状の減少を伴う緩やかな改善が認められた（身体外部の炎症の指標の漸進的改善）。被験者は鉄欠乏性貧血も発現し，フェインジェクトの静脈内投与を受けた。直腸・S 字結腸鏡検査が行われたが，内視鏡下では改善が認められなかった。結腸全摘術が予定された。被験者の不安のため，心理学的及び精神的評価が開始された。投与73日後＊　，被験者は退院した。

投与80日後＊　，被験者は潰瘍性大腸炎の進行，血性下痢及び腹痛のため再入院した。同日，被験者は回腸瘻造設を伴う結腸切除術を受けた。投与81日後＊　，被験者は腹部 CT スキャン検査を受け，腸の膨満が認められたが，穿孔は認められなかった。投与87日後＊　，被験者は良好な状態で退院した。

この被験者の治験は中止された。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

MESALAZINE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

GOLIMUMAB for ULCERATIVE COLITIS ([redacted])

BUDESONIDE MMX for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.23.0]　[10009901]

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

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

Dechallenge: Not Applicable

2)Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.23.0]　[10009901]

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 WORSENING OF ULCERATIVE COLITIS

- Investigator: EXACERBATION OF THE DISEASE

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

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: PROGRESSION OF DISEASE

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL CT SCAN:** Bowel distension, no perforation

[redacted] **BLOOD ANTIGENE ADENOVITRUS RESEARCH RAPID TEST:** NEGATIVE.

[redacted] **BLOOD ANTIGENE ROTAVIRUS RESEARCH RAPID TEST:** NEGATIVE.

[redacted] **20[redacted] BLOOD UREA:** 1.8 MMOL/L (normal 2.9 to 8.2)

[redacted] **20[redacted] BLOOD UREA:** 2.4 MMOL/L (normal 2.9 to 8.2)

[redacted] **20[redacted] COLONOSCOPY:** A clear demarcation between normal and inflamed colonic mucosa was seen. The distance of demarcation from the anal verge was 50, and the Central Reader Endoscopy Subscore was 3.

[redacted] **20[redacted] COMPLETE ABDOMEN ECOGRAPHY:** THERE IS EVIDENCE OF THICKENING OF THE WALLS OF THE DESCENDANT AND OF THE SIGMA WITH MODEST HYPEREMIA AT DOPPLER, TO BE COMPARED TO INFLAMMATORY PHENOMENA (KNOWN PICTURE OF ULCERATIVE RECTOCOLITIS).

[redacted] **20[redacted] CRP:** 122.58 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 20.82 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 39 MG/L (normal 0 to 5)

[redacted] **20[redacted] EOSINOPHILS ABS:** 0.6 X10**9/L (normal 0 to 0.45)

[redacted] **20[redacted] EOSINOPHILS ABS:** 0.6 X10**9/L (normal 0 to 0.45)

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** A clear demarcation between normal and inflamed colonic mucosa was not seen. No normal mucosa (pancolitis).

[redacted] **20[redacted] HEMATOCRIT:** 0.32 L/L (normal 0.42 to 0.52)

[redacted] **20[redacted] HEMATOCRIT:** 0.34 L/L (normal 0.42 to 0.52)

[redacted] **20[redacted] HEMOGLOBIN:** 108 G/L (normal 140 to 180)

[redacted] **20[redacted] HEMOGLOBIN:** 109 G/L (normal 140 to 180)

[redacted] **20[redacted] HEMOGLOBIN:** 116 G/L (normal 140 to 180)

[redacted] **20[redacted] HEMOGLOBIN:** 110 G/L (normal 140 to 180)

[redacted] **20[redacted] IRON:** 4.1 MMOL/L (normal 11.64 to 31.33)

[redacted] **20[redacted] PLAIN ABDOMINAL RADIOGRAPHY:** NORMAL

[redacted] **20[redacted] PLASMA TEST:** CITOMEGALOVIRUS SEQUENCES DNA RESEARCH - NEGATIVE.

[redacted] **20[redacted] RECTOSIGMOIDOSCOPY:** No endoscopic improvement

[redacted] **20[redacted] SIGMA (A) AND RECTUM (B) BIOPSIES:** POSITIVE- MUCOUS MEMBRANE OF THE LARGE INTESTINE WITH ARCHITECTURAL DISTORTION AND WITH CHRONIC ACTIVE INFLAMMATION WITH AN ULCERATIVE FOOTPRINT (A), WITH CHRONIC ACTIVE EROSIVE

PHLOGOSIS (B).

[redacted] **20[redacted] STOOL TEST:** CLOSTRIDIUM DIFFICILE - NEGATIVE

[redacted] **20[redacted] STOOL TEST:** COPROPARASSITOLOGICAL EXAMINATION - NEGATIVE

[redacted] **20[redacted] STOOL TEST:** YERSINIA - NEGATIVE.

[redacted] **20[redacted] STOOL TEST:** COPROPARASSITOLOGICAL EXAMINATION - NEGATIVE. SEVERAL WHITE BLOOD CELLS

[redacted] **20[redacted] STOOL TEST:** COPROPARASSITOLOGICAL EXAMINATION - NEGATIVE. SOME WHITE BLOOD CELLS AND SEVERAL BLASTOSPORES

[redacted] **20[redacted] URINE UREA:** 39.62 MMOL/L (normal 141 to 494)

[redacted] **20[redacted] URINE UREA:** 74.24 MMOL/L (normal 141 to 494)

[redacted] **20[redacted] URINE UREA:** 104.8 MMOL/L (normal 141 to 494)

[redacted] **20[redacted] WEIGHT:** 8[redacted] KG

[redacted] **20[redacted] WHITE BLOOD CELLS:** 18 X10**9/L (normal 5.2 to 12.4)

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
P1:ABT-494 45 mg	2[redacted]	FEMALE	ASIAN

Medical History	Onset Year
ASTHMA	20[redacted]
LEFT SIDED UC	20[redacted]
SACRAL PAIN	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2 - 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -165
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted] / -166
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -93
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -56
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -56
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -72
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -42
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 L	QD	Y-M: 20[redacted] / -8
BIFIDOBACTERIUM LACTIS	1 g	TID	Y-M: 20[redacted] / -8
DIMETICONE	5 mL	QD	Y-M: 20[redacted] / -8
FLUNITRAZEPAM	2 mg	QD	Y-M: 20[redacted] / -8
LIDOCAINE	10 mL	QD	Y-M: 20[redacted] / -8
MOSAPRIDE	10 mg	QD	Y-M: 20[redacted] / -8
PETHIDINE	1 mL	QD	Y-M: 20[redacted] / -8
SODIUM BICARBONATE	500 mL	QD	Y-M: 20[redacted] / -8
SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / -9

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -165	ONGOING
PARACETAMOL	200 mg	PRN	Y-M: 20[redacted] / 16	ONGOING
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 30
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 36
TIPEPIDINE	20 mg	TID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 36
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 40
CAFFEINE;PARACETAMOL;PROMETHAZINE;SALICYLAMIDE	1 g	TID	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 55
DEQUALINIUM	0.25 mg	PRN	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 63
MICONAZOLE	PROPER QUANTITY OTHER:	TID	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 84

	N/A			
SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 55
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 L	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
DIMETICONE	2.5 mL	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
FAMOTIDINE	2 mL	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
FLOMOXEF	1 g	BID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 58
GLUCOSE	250 mL	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
HEPARIN	5 mL	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 58
MAGNESIUM CITRATE	50 g	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 56
POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
SODIUM BICARBONATE	500 mL	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 56
ACETYLCYSTEINE;ALANINE;ARGININE;ASCORBIC ACID;ASPARTIC ACID;BIOTIN;CALCIUM CHLORIDE;CYANOCOBALAMIN;FOLIC ACID;GLUCOSE;GLUTAMIC ACID;GLYCINE;HISTIDINE;ISOLEUCINE;LEUCINE;LYSINE;MAGNESIUM SULFATE;METHI	500 mL	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 58
FLUNITRAZEPAM	2 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
LIDOCAINE	10 mL	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
MOSAPRIDE	10 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
PENTAZOCINE	15 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
PETHIDINE	1 mL	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 62

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

Event Description	APPENDICITIS
Preferred term	虫垂炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 56 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 56): Leukocytes: 13.72 [3.5 - 9.7] 10^9/L; NPTST159-CRP: 0.95 [0 - 0.3] MG/DL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 56): ABDOMINAL CT EXAMINATION: APPENDICITIS SUSPECTED SUSPECTED GALLBLADDER ADENOMYOMATOSIS

AE Stopped Rx Day	63 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，虫垂炎の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），非喫煙者及び少量の現飲酒者であった。

Event 1 の臨床経過：

投与56日後＊，被験者は虫垂炎を発現した。投与63日後＊，虫垂炎は消失した。

本事象発現の 1 週間前，被験者は感冒（非重篤）を患っていた。

投与55日後＊　　，被験者は発熱及び嘔吐を経験した。投与56日後＊　　，被験者は発熱及び嘔吐に加えて，胃痛を訴えた。血液学的所見に基づき，血液検査及び CT スキャン検査を完了した。被験者は当初，「感冒性胃腸炎」と診断され，抗生物質の投与が開始され，内視鏡検査が計画された。投与56日後＊　　，被験者は観察下で入院した。投与57日後＊　　，内視鏡検査で虫垂炎が確認され，抗生物質の投与が継続された。被験者の症状は重症ではなかったため，被験者は投与58日後＊　　に退院した。投与63日後＊　　，来院にて経過観察を行ったところ，被験者は圧痛を訴えたが，血液検査は炎症の減少を示していた。

投与された薬剤は，ソリタ−T 配合顆粒 3 号，ソセゴン，パレプラス輸液，ヘパリン Na，クラビット，ガスター，ブドウ糖及びフルマリンであった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1) Appendicitis (10003011) (Appendicitis (10003011)) [v.23.0] [10003011]

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 APPENDICITIS

- Investigator: Bacterial infectious disorders

- AbbVie: Event is common in the general population; lifetime incidence is 8.6 percent in males and 6.7 percent in females.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ABDOMINAL CT:** Appendicitis suspected, suspected gallbladder adenomyomatosis

[redacted] 20[redacted] **CRP:** 0.95 mg/dL (normal 0 to 0.3)

[redacted] 20[redacted] **ENDOSCOPY:** Appendicitis.

[redacted] 20[redacted] **WBC:** 13.72 X10**3/MCL (normal 3.5 to 9.7)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
慢性腎臓病		X		
前立腺特異性抗原増加				X
発熱	X	X		

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 45 mg	7[redacted]	MALE	ASIAN

Medical History	Onset Year
ANGINA PECTORIS	20[redacted]
CHRONIC KIDNEY DISEASE	20[redacted]
COLON POLYPS	NOT REPORTED
DYSLIPIDAEMIA	20[redacted]
GONALGIA	20[redacted]
HYPERTENSION	19[redacted]
LEFT SIDED UC	20[redacted]
PROSTATIC HYPERTROPHY	20[redacted]
TUBLAR ADENOMA(S-COLON)	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: CORONARY STENT PLACEMENT(RIGHT)	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: COLON POLYPECTOMY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	36	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 22	22

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]-[redacted]
SULFASALAZINE	500 mg	QD	Y-M: 20[redacted]-[redacted]
BETAMETHASONE	3 g	PRN	Y-M: 20[redacted]-[redacted]
MESALAZINE	1 g	PRN	Y-M: 20[redacted]-[redacted]
SULFASALAZINE	2000 mg	BID	Y-M: 20[redacted]-[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted]-[redacted]
SULFASALAZINE	500 mg	PRN	Y-M: 20[redacted]-[redacted]
MESALAZINE	1 g	PRN	Y-M: 20[redacted]-[redacted]
PREDNISOLONE	2 g	PRN	Y-M: 20[redacted]-[redacted]
METRONIDAZOLE	500 mg	PRN	Y-M: 20[redacted]-[redacted]
BETAMETHASONE	1 mg	PRN	Y-M: 20[redacted]-[redacted]
MESALAZINE	1 g	PRN	Y-M: 20[redacted]-[redacted]
MESALAZINE	3200 mg	BID	Y-M: 20[redacted]-[redacted]
MESALAZINE	1 g	PRN	Y-M: 20[redacted]-[redacted]
MESALAZINE	1 g	PRN	Y-M: 20[redacted]-[redacted]
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted]-[redacted]
LANSOPRAZOLE	15 mg	QD	Y-M: 20[redacted]-[redacted]
APIXABAN	5 mg	BID	Y-M: 20[redacted]-[redacted]
BUDESONIDE	2 mg	PRN	Y-M: 20[redacted]-[redacted]
MESALAZINE	1 g	PRN	Y-M: 20[redacted]-[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]-[redacted]
BETAMETHASONE	3 mg	PRN	Y-M: 20[redacted]-[redacted] / -234
BETAMETHASONE	1 mg	PRN	Y-M: 20[redacted]-[redacted] / -238
TAMSULOSIN	0.2 mg	QD	Y-M: 20[redacted]-[redacted] / -135
ROSUVASTATIN	5 mg	QD	Y-M: 20[redacted]-[redacted] / -

			104
APIXABAN	5 mg	BID	Y-M: 20[redacted] / -5
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted] / -6
BENFOTIAMINE;CYANOCOBALAMIN;PYRIDOXINE	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / -6
CARBAZOCHROME	100 mg	QD	Y-M: 20[redacted] / -6
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACKAGE	QD	Y-M: 20[redacted] / -7
GLUCOSE;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	TID	Y-M: 20[redacted] / -7
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -7
AMLODIPINE	2.5 mg	QD	Y: 20[redacted]
DILTIAZEM	100 mg	BID	Y: 20[redacted]
ISOSORBIDE MONONITRATE	20 mg	BID	Y: 20[redacted]
OLMESARTAN	20 mg	QD	Y: 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	100 mg	QD	Y-M: 20[redacted]	ONGOING
LANSOPRAZOLE	15 mg	QD	Y-M: 20[redacted]	ONGOING
APIXABAN	5 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / -8
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]	ONGOING
TAMSULOSIN	0.2 mg	QD	Y-M: 20[redacted] / -135	ONGOING
ROSUVASTATIN	5 mg	QD	Y-M: 20[redacted] / -104	ONGOING
APIXABAN	5 mg	BID	Y-M: 20[redacted] / -5	ONGOING
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted] / -6	Y-M: 20[redacted] / -5
BENFOTIAMINE;CYANOCOBALAMIN; PYRIDOXINE	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / -6	Y-M: 20[redacted] / -5
CARBAZOCHROME	100 mg	QD	Y-M: 20[redacted] / -6	Y-M: 20[redacted] / -5
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACKAGE	QD	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -7
GLUCOSE;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	TID	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -4
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -7
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted] / 12	ONGOING
BISACODYL	10 mg	PRN	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 26
DIFLUCORTOLONE;LIDOCAINE	PRN g	PRN	Y-M: 20[redacted] / 22	ONGOING

GLYCEROL	120 mL	PRN	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 26
MAGNESIUM OXIDE	660 mg	PRN	Y-M: 20[redacted] / 22	ONGOING
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 28
BENFOTIAMINE;CYANOCOBALAMIN; PYRIDOXINE	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 28
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 26
GLUCOSE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 28
GLUCOSE;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 28
NADIFLOXACIN	PRN g	PRN	Y-M: 20[redacted] / 26	ONGOING
AMLODIPINE	2.5 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 9
DILTIAZEM	100 mg	BID	Y: 20[redacted]	ONGOING
ISOSORBIDE MONONITRATE	20 mg	BID	Y: 20[redacted]	ONGOING
OLMESARTAN	20 mg	QD	Y: 20[redacted]	ONGOING

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

Event Description	FEVER
Preferred term	発熱
AE Onset Date / Rx Day	[redacted]20[redacted] / 3
Age at AE Onset	7[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 22): Creatinine: 143.213281 [57.462119 - 94.591488] UMOL/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 28): CT: NO ABNORMALITY	
AE Stopped Rx Day	29 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	27 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	WORSENING OF CHRONIC KIDNEY DISEASE
Preferred term	慢性腎臓病
AE Onset Date / Rx Day	[redacted]20[redacted] / 22
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	28 (6 DAYS AFTER LAST TREATMENT)
Duration of AE	7 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #3: Event of Interest - Possible Malignancies

Event Description	PSA INREASED
Preferred term	前立腺特異性抗原増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 48 (26 DAYS AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO

SAE Criteria NONE

Generated: [redacted]20[redacted]:10:36
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，発熱の事象を発現した。関連する病歴は，高血圧，潰瘍性大腸炎，慢性腎臓病，脂質異常症，元喫煙者（1 日 1 箱を 36 年間）及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与3日後＊ ，被験者は発熱を発現した。投与29日後＊ ，発熱は消失した。

投与22日後＊ ，被験者は摂氏 38°C の発熱があり，クリニックを受診した。臨床検査の結果，発熱は感染によるものではないと判断され，治験薬との関連が考えらえた。その後，治験薬の投与は中止された。投与26日後＊ ，被験者は発熱でクリニックを再受診し，輸液療法のため入院した。臨床検査結果は今回も正常であった。投与27日後＊ ，被験者の体温は摂氏 36.4°C に下がり，倦怠感も改善していた。投与28日後＊ ，被験者の体温は摂氏 36°C 付近で安定した。投与29日後＊ ，被験者は良好な経過で退院した。

投与された薬剤は，ソルデム 1 輸液，ラクテック，ソルアセト D 輸液，アスコルビン酸及びビタメジンであった。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS ([redacted])

SALAZOPYRIN for ULCERATIVE COLITIS ([redacted])

STERONEMA for ULCERATIVE COLITIS ([redacted])

SALAZOPYRIN for ULCERATIVE COLITIS ([redacted])

PREDONEMA for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

RINDERON for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

RECTABUL for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Fever (10016558) (Pyrexia (10037660)) [v.23.0] [10016558]

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 FEVER

- Investigator: Not applicable

- AbbVie: Event is common in the general population. Ulcerative colitis is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

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

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

[redacted] **20[redacted] CREATININE:** 1.24 mg/dL

[redacted] **20[redacted] CT SCAN:** No abnormalities.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血				X
低アルブミン血症	X			

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo /P2:ABT-494 45 mg	7[redacted]	MALE	ASIAN

Medical History	Onset Year
ADRENAL ADENOMA	NOT REPORTED
ANEMIA	20[redacted]
ARTHRITIS	20[redacted]
EPISCLERITIS	20[redacted]
EXTENSIVE UC/PANCOLITIS	19[redacted]
HYPERTENSION	NOT REPORTED
HYPERURICEMIA	NOT REPORTED
INGUINAL HERNIA	NOT REPORTED
MITRAL REGURGITATION	NOT REPORTED
NEUTROPHILIC DERMATOSES	20[redacted]
PULMONARY EMPHYSEMA	NOT REPORTED
SCALP RASH	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	25	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo			[redacted] / 1	[redacted] / 56	56
ABT-494 45 mg	45 mg	QD	[redacted] / 57	0[redacted] / 112	56

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	500 mg	TID	Y-M: 19[redacted]
BUDESONIDE	2 mg	QD	Y-M: 20[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	TID	Y-M: 20[redacted]
OTHER THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: [redacted]	Y-M: 20[redacted]
OTHER THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: [redacted]	Y-M: 20[redacted]
PREDNISOLONE	20 mg	TID	Y-M: 20[redacted]
GOLIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	QD	Y-M: 20[redacted]
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted]
IRON	105 mg	BID	Y-M: 20[redacted]
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted] / -293
PREDNISOLONE	20 mg	BID	Y-M: 20[redacted] / -271
PREDNISOLONE	30 mg	OTHER: UNKNOWN	Y-M: 20[redacted] / -195
URSODEOXYCHOLIC ACID	200 mg	TID	Y-M: 20[redacted] / -190
PREDNISOLONE	30 mg	OTHER: UNKNOWN	Y-M: 20[redacted] / -126
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -42
CLOSTRIDIUM BUTYRICUM	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -42
BETAMETHASONE	1 OTHER: DROP	PRN	Y-M: 20[redacted] / -14
LEVOFLOXACIN	1 OTHER: DROP	PRN	Y-M: 20[redacted] / -14
IRON	315 mg	QD	Y-M: 20[redacted] / -21

BETAMETHASONE;NEOMYCIN	1 OTHER: DROP	OTHER: 8 TIMES A DAY	Y-M: 20[redacted] / -24
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	QD	Y-M: 20[redacted] / -31
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / -31
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -32
CAMPHOR;MENTHOL;SALICYLIC ACID	40 g	PRN	Y-M: 20[redacted] / -37
PARACETAMOL	200 mg	TID	Y-M: 20[redacted] / -37
FLAVINE ADENINE DINUCLEOTIDE	1 OTHER: DROP	OTHER: 4 TIMES A DAY	Y-M: 20[redacted] / -40
FLUOROMETHOLONE	1 OTHER: DROP	OTHER: 4 TIMES A DAY	Y-M: 20[redacted] / -40
MOXIFLOXACIN	1 OTHER: DROP	OTHER: 4 TIMES A DAY	Y-M: 20[redacted] / -40

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
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 156
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 156
URSODEOXYCHOLIC ACID	200 mg	TID	Y-M: 20[redacted] / -190	ONGOING
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -42	Y-M: 20[redacted] / 1
CLOSTRIDIUM BUTYRICUM	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -42	ONGOING
BETAMETHASONE	1 OTHER: DROP	PRN	Y-M: 20[redacted] / -14	ONGOING
LEVOFLOXACIN	1 OTHER: DROP	PRN	Y-M: 20[redacted] / -14	ONGOING
IRON	315 mg	QD	Y-M: 20[redacted] / -21	Y-M: 20[redacted] / 34
NUTRIENTS NOS	250 mL	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 29
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 33
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	BID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 33

GUAIAZULENE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 41
HEPARINOID	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 126
ALBUMIN HUMAN	100 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 38
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 37
BENFOTIAMINE;CYANOCOBALAMIN;PYRIDOXINE	1 OTHER: VIAL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
CALCIUM CHLORIDE;GLUCOSE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
GLUCOSE	100 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 43
GLUCOSE	500 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
GLYCINE MAX	250 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
HEPARIN	10 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
IRON	40 mg	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 43
MAGNESIUM SULFATE	1 mEq	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 40
POTASSIUM	20 mEq	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 36
SODIUM CHLORIDE	20 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 61
GLYCINE MAX	250 mL	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 75
HEPARIN	10 mL	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 75
AMINO ACIDS NOS;COPPER;ELECTROLYTES NOS;GLUCOSE;IODINE;IRON;MANGANESE;VITAMINS NOS;ZINC	1500 mL	QD	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 39
POTASSIUM	20 mEq	QD	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 47
AMINO ACIDS NOS;COPPER;ELECTROLYTES NOS;GLUCOSE;IODINE;IRON;MANGANESE;VITAMINS NOS;ZINC	1500 mL	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 61
GLUCOSE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 68
SODIUM PHOSPHATE	20 mL	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 68
ALBUMIN HUMAN	100 mL	QD	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 43
RED BLOOD CELLS	2 OTHER: U	QD	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 41

WHITE SOFT PARAFFIN	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: FOUR TIMES A DAY	Y-M: 20[redacted] / 41	ONGOING
ZINC	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: FOUR TIMES A DAY	Y-M: 20[redacted] / 41	ONGOING
CALCIUM GLUCONATE	5 mL	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 50
MAGNESIUM SULFATE	1 mEq	QD	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 47
RED BLOOD CELLS	2 OTHER: U	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 47
POTASSIUM	10 mEq	QD	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 50
ALBUMIN HUMAN	100 mL	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 54
GLUCOSE	100 mL	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 54
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 51
IRON	40 mg	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 54
PARACETAMOL	400 mg	BID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 53
CEFOZOPRAN	1 g	BID	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 61
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 57
RED BLOOD CELLS	2 OTHER: U	QD	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 54
POTASSIUM	20 mEq	QD	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 64
ALBUMIN HUMAN	50 mL	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 64
AMINO ACIDS NOS;COPPER;ELECTROLYTES NOS;GLUCOSE;IODINE;IRON;MANGANESE;VITAMINS NOS;ZINC	1000 mL	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 64
SELENIUM	100 ug	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 68
GLUCOSE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 68
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 69
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 75	Y-M: 20[redacted] / 77
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 110
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 110
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 84
HEPARINOID	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: TWICE OR THREE TIMES A DAY	Y-M: 20[redacted] / 127	ONGOING

LULICONAZOLE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	QD	Y-M: 20[redacted] / 127	ONGOING
ALCLOMETASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: TWICE OR THREE TIMES A DAY	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 162
BETAMETHASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: TWICE OR THREE TIMES A DAY	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 162
LEVOCETIRIZINE	2.5 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / 158	Y-M: 20[redacted] / 160
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / 158	Y-M: 20[redacted] / 160
LEVOCETIRIZINE	2.5 mg	QD	Y-M: 20[redacted] / 162	ONGOING
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 162	ONGOING

Event #1: Serious Adverse Event

Event Description	HYPOALBUMINEMIA
Preferred term	低アルブミン血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 29
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 29): Albumin: 16 [41 - 51] G/L; [redacted]20[redacted] (RX DAY 33): Albumin: 14 [41 - 51] G/L; [redacted]20[redacted] (RX DAY 82): Albumin: 34 [41 - 51] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 33): PERIPHERALLY INSERTED CENTRAL CATHETER: INTRAVENOUS NUTRITION WAS STARTED.

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DUE TO ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION,

IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #2: Event of Interest - Anemia

Event Description	WORSENING OF ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 41
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	57
Duration of AE	17 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:36
Program Source Code: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 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，低アルブミン血症の事象を発現した。関連する病歴は，潰瘍性大腸炎及び貧血であった。

Event 1 の臨床経過：

投与29日後＊ ，被験者は低アルブミン血症を発現した。

投与29日後＊　　，被験者は低アルブミン血症のため入院した。被験者は食事の摂取を中止し，静脈栄養を開始した。被験者は末梢性浮腫，全身疲労及び食欲不振を経験した。　　投与33日後＊，末梢穿刺中心静脈カテーテル（PICC）が挿入され高カロリー輸液が投与された。　投与41日後＊　，被験者は経口での食事の摂取を開始した。投与75日後＊　　，静脈栄養を終了した。投与86日後＊　，被験者は退院した。

入院中，被験者は肛門粘膜炎，発熱及び体重減少（すべて非重篤）を発現した。

投与された薬剤は，ブドウ糖，ソリューゲン F，ソルデム 3A，硫酸マグネシウム，ヴィーン D，ビタメジン，エルネオパ NF2 号，リン酸ナトリウム，デノサリン，カルチコール，ベルベゾロン F，アセレンド，ソリタックス−H，ソルデム 3A，アルクロメタゾンプロピオン酸エステル，ベタメタゾン酪酸エステルプロピオン酸エステル，塩化カリウム，塩化ナトリウム，ビーフリード，アルブミン，イントラリポス及びエルネオパ NF1 号であった。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

RECTABUL for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

CELLSORBA for ULCERATIVE COLITIS ([redacted])

SIMPONI for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Hypoalbuminemia (10020943)　(Hypoalbuminaemia (10020942))　[v.24.0]　[10020943]

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 HYPOALBUMINEMIA

- Investigator: Due to ulcerative colitis.

- AbbVie: Risk factor includes pre-existing Ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 1.6 G/DL (normal 4.1 to 5.1)

[redacted] **20[redacted] ALBUMIN:** 1.4 G/DL (normal 4.1 to 5.1)

[redacted] **20[redacted] ALBUMIN:** 3.4 G/DL

[redacted] **20[redacted] ALBUMIN- BCG:** 3.4 G/DL (normal 3.3 to 4.6)

[redacted] **20[redacted] ALBUMIN- BCG:** 3.7 G/DL (normal 3.3 to 4.6)

[redacted] **20[redacted] ALBUMIN- BCG:** 2.6 G/DL (normal 3.3 to 4.6)

[redacted] **20[redacted] ALBUMIN- BCG:** 2.2 G/DL (normal 3.3 to 4.6)

[redacted] **20[redacted] ALBUMIN- BCG:** 3.8 G/DL (normal 3.3 to 4.6)

[redacted] **20[redacted] ALBUMIN- BCG:** 3.7 G/DL (normal 3.3 to 4.6)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 63 U/L (normal 35 to 130)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 53 U/L (normal 35 to 130)

[redacted] **20[redacted] ALT (SGPT):** 4 U/L (normal 6 to 35)

[redacted] **20[redacted] ALT (SGPT):** 6 U/L (normal 6 to 35)

[redacted] **20[redacted] ALT (SGPT):** 7 U/L (normal 6 to 35)

[redacted] **20[redacted] ALT (SGPT):** 9 U/L

[redacted] **20[redacted] ALT (SGPT):** 13 U/L (normal 6 to 35)

[redacted] **20[redacted] ALT (SGPT):** 5 U/L (normal 6 to 35)

[redacted] **20[redacted] ALT (SGPT):** 4 U/L (normal 6 to 35)

[redacted] **20[redacted] AST (SGOT):** 10 U/L (normal 11 to 36)

[redacted] **20[redacted] AST (SGOT):** 10 U/L (normal 11 to 36)

[redacted] **20[redacted] AST (SGOT):** 10 U/L (normal 11 to 36)

[redacted] **20[redacted] AST (SGOT):** 13 U/L (normal 11 to 36)

[redacted] **20[redacted] AST (SGOT):** 13 U/L (normal 11 to 36)

[redacted] **20[redacted] AST (SGOT):** 12 U/L(normal 11 to 36)

[redacted] **20[redacted] AST (SGOT):** 12 U/L (normal 11 to 36)

Unknown date CHEST X-RAY: Screening: Bilateral LUNG SHOWS EMPHYSEMATOUS CHANGES. THERE IS A SCAR IN THE UPPER RIGHT LUNG FIELD.

[redacted] **20[redacted] ENDOSCOPY:** Unknown

[redacted] **20[redacted] GGT:** 10 U/L (normal 10 to 50)

[redacted] **20[redacted] GGT:** 14 U/L (normal 10 to 50)

[redacted] **20[redacted] GGT:** 11 U/L (normal 10 to 50)

[redacted] **20[redacted] GGT:** 7 U/L

[redacted] **20[redacted] GGT:** 6 U/L (normal 10 to 50)

[redacted] **20[redacted] GGT:** 7 U/L (normal 10 to 50)

[redacted] **20[redacted] GGT:** 6 U/L (normal 10 to 50)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 0.4 mg/dL (normal 0.2 to 1.2)

[redacted] **20[redacted] TOTAL BILIRUBIN:** <0.2 mg/dl

[redacted] **20[redacted] TOTAL BILIRUBIN:** 0.2 mg/dL (normal 0.2 to 1.2)

[redacted] **20[redacted] TOTAL BILIRUBIN:** <0.2 mg/dl

[redacted] **20[redacted] TOTAL BILIRUBIN:** 0.2 mg/dL (normal 0.2 to 1.2)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 0.2 mg/dL (normal 0.2 to 1.2)

[redacted] **20[redacted] TOTAL PROTEIN:** 6.3 G/DL (normal 6.0 to 8.0)

[redacted] **20[redacted] TOTAL PROTEIN:** 5.0 G/DL (normal 6.0 to 8.0)

[redacted] **20[redacted] UR CLARITY:** Hazy

[redacted] **20[redacted] URINE NITRITE:** Negative

[redacted] **20[redacted] URINE PH:** 6.0 No units (normal 5.0 to 8.0)

[redacted] **20[redacted] URINE PROTEIN:** +2 Negative

[redacted] **20[redacted] URINE BILIRUBIN:** Negative

[redacted] **20[redacted] URINE BILIRUBIN:** Negative

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

[redacted] **20[redacted] URINE COLOR:** Yellow

[redacted] **20[redacted] URINE GLUCOSE:** Normal

[redacted] **20[redacted] URINE KETONES:** Negative

[redacted] **20[redacted] URINE LEUKOCYTE ESTERASE:** +3 Negative

[redacted] **20[redacted] URINE SPECIFIC GRAVITY:** 1.024 No units (normal 1.006 to 1.030)

[redacted] **20[redacted] URINE UROBILINOGEN:** 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
貧血				X
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 45 mg	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ACNE VULGARIS	NOT REPORTED
DRY SKIN	NOT REPORTED
LEFT SIDED UC	20[redacted]
POLLINOSIS	20[redacted]
SKIN ERUPTION	NOT REPORTED
WORSENING OF UC	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 5	5

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]
BUDESONIDE	2 mg	BID	Y-M: 20[redacted] / -75
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	QID	Y-M: 20[redacted] / -27
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	TID	Y-M: 20[redacted] / -28
GLYCINE MAX	100 mL	QD	Y-M: 20[redacted] / -28
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -28
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / -29
GLYCEROL	60 mL	QD	Y-M: 20[redacted] / -29
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	QD	Y-M: 20[redacted] / -30
GLUCOSE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1000 mL	QD	Y-M: 20[redacted] / -30
ALFACALCIDOL	0.5 ug	QD	Y-M: 20[redacted] / -33
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -33
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted] / -33
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	OTHER: TWO TIMES PER WEEK (BID)	Y-M: 20[redacted] / -33
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -40
MESALAZINE	1 g	QD	Y-M: 20[redacted] / -40
MESALAZINE	2000 mg	BID	Y-M: 20[redacted] / -40
AMINO ACIDS NOS;CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;VITAMINS NOS	80 g	QD	Y-M: 20[redacted] / -19
CLOBETASOL	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -3

BETAMETHASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -5
DEXAMETHASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -5
PARACETAMOL	600 mg	PRN	Y-M: 20[redacted] / -6
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / -7
DIMETICONE	5 mL	QD	Y-M: 20[redacted] / -7
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	2000 mL	PRN	Y-M: 20[redacted] / -7
MIDAZOLAM	2 mL	QD	Y-M: 20[redacted] / -7
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted] / -8
SENNOSIDE A+B	24 mg	PRN	Y-M: 20[redacted] / -8
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	QID	Y-M: 20[redacted] / -27	Y-M: 20[redacted] / -14
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	TID	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / -28
GLYCINE MAX	100 mL	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / -15
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -28	Y-M: 20[redacted] / 19
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / -29	Y-M: 20[redacted] / -29
GLYCEROL	60 mL	QD	Y-M: 20[redacted] / -29	Y-M: 20[redacted] / -29
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	QD	Y-M: 20[redacted] / -30	Y-M: 20[redacted] / -29
GLUCOSE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1000 mL	QD	Y-M: 20[redacted] / -30	Y-M: 20[redacted] / -28
ALFACALCIDOL	0.5 ug	QD	Y-M: 20[redacted] / -33	Y-M: 20[redacted] / 14
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -33	Y-M: 20[redacted] / -9
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted] / -33	Y-M: 20[redacted] / 9

SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	OTHER: TWO TIMES PER WEEK (BID)	Y-M: 20[redacted] / -33	Y-M: 20[redacted] / -29
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -40	ONGOING
MESALAZINE	2000 mg	BID	Y-M: 20[redacted] / -40	Y-M: 20[redacted] / 10
AMINO ACIDS NOS;CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;VITAMINS NOS	80 g	QD	Y-M: 20[redacted] / -19	Y-M: 20[redacted] / -9
CLOBETASOL	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -3	Y-M: 20[redacted] / 2
BETAMETHASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -5	Y-M: 20[redacted] / -3
DEXAMETHASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -5	Y-M: 20[redacted] / 2
PARACETAMOL	600 mg	PRN	Y-M: 20[redacted] / -6	Y-M: 20[redacted] / -6
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -7
DIMETICONE	5 mL	QD	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -7
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	2000 mL	PRN	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -7
MIDAZOLAM	2 mL	QD	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -7
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted] / -8	Y-M: 20[redacted] / 12
SENNOSIDE A+B	24 mg	PRN	Y-M: 20[redacted] / -8	Y-M: 20[redacted] / -8
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -8	Y-M: 20[redacted] / -8
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
GLUCOSE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1000 mL	BID	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 9
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	TID	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 2

HEPARINOID	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / 2	ONGOING
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	QD	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 3
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 3
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	BID	Y-M: 20[redacted] / 4	Y-M: 20[redacted] / 9
CEFMETAZOLE	1 g	QD	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 5
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 10
CEFMETAZOLE	1 g	BID	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 8
METHYLPREDNISOLONE	500 mg	QD	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 8
POTASSIUM	20 mL	QD	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 8
KETOCONAZOLE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	QD	Y-M: 20[redacted] / 8	ONGOING
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 9
CEFMETAZOLE	1 g	BID	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 9
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 18
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	OTHER: 6 TIMES A DAY	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 12
CEFMETAZOLE	1 g	TID	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 12
INFLIXIMAB	250 mg	QD	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 10
METHYLPREDNISOLONE	125 mg	QD	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 10
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 19
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 10
AMINO ACIDS NOS;COPPER;ELECTROLYTES NOS;GLUCOSE;IODINE;IRON;MANGANESE; VITAMINS NOS;ZINC	1000 mL	QD	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 12
BETAMETHASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / 12	ONGOING

DEXAMETHASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / 12	ONGOING
MENATETRENONE	10 mg	QD	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 12
AMINO ACIDS NOS;COPPER;ELECTROLYTES NOS;GLUCOSE;IODINE;IRON;MANGANESE; VITAMINS NOS;ZINC	1000 mL	TID	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 13
AMINO ACIDS NOS;COPPER;ELECTROLYTES NOS;GLUCOSE;IODINE;IRON;MANGANESE; VITAMINS NOS;ZINC	1000 mL	BID	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 21
OLOPATADINE	10 mg	BID	Y-M: 20[redacted] / 14	ONGOING
GUAIAZULENE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	PRN	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 22
INFLIXIMAB	250 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 16
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 16
CLOBETASOL	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / 19	ONGOING
GLYCINE MAX	100 mL	QD	Y-M: 20[redacted] / 19	ONGOING
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 23
WHITE SOFT PARAFFIN	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / 19	ONGOING
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted] / 20	ONGOING
AMINO ACIDS NOS;COPPER;ELECTROLYTES NOS;GLUCOSE;IODINE;IRON;MANGANESE; VITAMINS NOS;ZINC	1500 mL	QD	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 22
AMINO ACIDS NOS;COPPER;ELECTROLYTES NOS;GLUCOSE;IODINE;IRON;MANGANESE; VITAMINS NOS;ZINC	1000 mL	BID	Y-M: 20[redacted] / 23	ONGOING

HEPARIN	1000 OTHER: U	OTHER: 3TIMES A WEEK	Y-M: 20[redacted] / 23	ONGOING
PREDNISOLONE	25 mg	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 26
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 29
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 32
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / 33	ONGOING
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
MIDAZOLAM	2 mL	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34

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

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 1
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 1): Leukocytes: 9.7 [3.3 - 8.6] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 1): CONTRAST-ENHANCED CT: CONTRAST-ENHANCED CT SHOWED INTESTINAL WOLL THICKENING, AND THE DESEASE BECAME PANCOLITIS TYPE UC.; [redacted]20[redacted] (RX DAY 34): ENDOSCOPY: ?THE MUCOUS MEMBRANE FROM THE RECTUM TO THE SIGMOID COLON IS BLEEDING WITH REDDISH TONE, AND EROSION AND WHITE MOSS ADHERE. ?THE MUCOUS MEMBRANE BLEEDS EASILY AND THE MAYO SCORE IS 3.

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RELAPSE OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Anemia

Event Description	ANAEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 19 (14 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:36
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 2[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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，潰瘍性大腸炎の悪化，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与初日＊　　，被験者は潰瘍性大腸炎の悪化を発現した。

投与初日＊　　，被験者は摂氏 39.6°C の発熱（非重篤）及び血便の悪化（1 日 10 回）のため病院を受診した。臨床検査では白血球数増加（非重篤），造影 CT 検査では腸壁の肥厚が認められ，全大腸炎型の潰瘍性大腸炎となっていた。被験者は潰瘍性大腸炎の悪化と診断され入院した。投与6日後＊　　，被験者はステロイドミニパルス療法で治療された。投与23日後＊　　，被験者は顆粒球吸着除去療法（GCAP）で治療された。

投与70日後＊　　，被験者はさらなる治療のため他院へ転院した。投与86日後＊　　，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。

投与された薬剤は，セフメタゾール Na，レミケード，ケイツー，プレドニン，メチルプレドニゾロンコハク酸エステルナトリウム，ヘパリン，ビーフリード，ソルデム，タクロリムス及びソルラクトであった。

The patient's past medications include:

LIALDA for ULCERATIVE COLITIS ([redacted])

RECTABUL for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

---

1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.23.0]　[10009901]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Relapse of ulcerative colitis.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY TEMPERATURE:** 39.6 Degrees C

[redacted] **20[redacted] COLONOSCOPY:** a clear demarcation between normal and inflamed colon mucosa was seen, 35cm from the anal verge

[redacted] **20[redacted] CONTRAST-ENHANCED CT:** showed intestinal wall thickening, and the disease became pancolitis type UC

[redacted] **20[redacted] ENDOSCOPY:** The mucous membrane from the rectum to the sigmoid colon is bleeding with reddish tone, and erosion and white moss adhere. The mucous membrane bleeds easily and the Mayo score is 3.

[redacted] **20[redacted] VIRAL TEST:** negative for influenza

[redacted] **20[redacted] WBC:** 9.7 10^3/uL (normal 3.3 to 8.6)

[redacted] **20[redacted] WBC:** 8.6 10^3/ul (normal 3.3 to 8.6)

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
リンパ球減少症				X
ウイルス感染	X	X		X

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 45 mg	6[redacted]	FEMALE	ASIAN

Medical History	Onset Year
IRON DEFICIENCY ANEMIA	20[redacted]
LEFT SIDED UC	20[redacted]
POST-MENOPAUSAL	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	40	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 51	51

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -242
IRON	50 mg	QD	Y-M: 20[redacted] / -119
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -20
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	122.106 g	PRN	Y-M: 20[redacted] / -7
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	PRN	Y-M: 20[redacted] / -7
DIMETICONE	200 mg	PRN	Y-M: 20[redacted] / -7
FLUMAZENIL	0.5 mg	PRN	Y-M: 20[redacted] / -7
MIDAZOLAM	4.0 mg	PRN	Y-M: 20[redacted] / -7
MOSAPRIDE	5 mg	PRN	Y-M: 20[redacted] / -7
SODIUM CHLORIDE	18 mL	PRN	Y-M: 20[redacted] / -7
MAGNESIUM CITRATE	34 g	PRN	Y-M: 20[redacted] / -8
SODIUM PICOSULFATE	75 mg	PRN	Y-M: 20[redacted] / -8
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19[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
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -242	ONGOING
IRON	50 mg	QD	Y-M: 20[redacted] / -119	ONGOING
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -20	ONGOING
OSELTAMIVIR	75 mg	BID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 58
PARACETAMOL	400 mg	TID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 58

Event #1: Event of Interest - Lymphopenia

Event Description	LYMPHOCYTEPENIA
Preferred term	リンパ球減少症
AE Onset Date / Rx Day	[redacted]20[redacted] / 45
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	64 (13 DAYS AFTER LAST TREATMENT)
Duration of AE	20 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	VIRAL INFECTION
Preferred term	ウイルス感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 51
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 62): Alanine Aminotransferase: 10 [7 - 23] U/L; Albumin: 29 [41 - 51] G/L; Alkaline Phosphatase: 148 [106 - 322] U/L; Aspartate Aminotransferase: 20 [13 - 30] U/L; Basophils/Leukocytes: 0.5 [0 - 1] %; Basophils/Leukocytes: 0.3 [0 - 2] %; Calcium: 2.045982 [2.195688 - 2.520051] MMOL/L; Creatine Kinase: 29 [41 - 53] U/L; Creatinine: 55.694054 [40.6655 - 69.838575] UMOL/L; Eosinophils: 0 [0 - 0.43] 10^9/L; Eosinophils/Leukocytes: 0 [2 - 5] %; Eosinophils/Leukocytes: 1 [1 - 4] %; Erythrocytes: 3390000 [3860000 - 4920000] mL; Glucose: 4.218532 [4.052011 - 6.050263] MMOL/L; Hematocrit: 0.306 [0.351 - 0.444] FRACTION OF 1; Hemoglobin: 102 [116 - 148] G/L; Leukocytes: 6.27 [3.3 - 8.6] 10^9/L; Lymphocytes: 1.59 [0.96 - 4.75] 10^9/L; Lymphocytes/Leukocytes: 25.4 [32 - 43] %; Lymphocytes/Leukocytes: 23 [20 - 44] %; Monocytes: 0.37 [0.1 - 0.97] 10^9/L; Monocytes/Leukocytes: 5.9 [3 - 6] %; Monocytes/Leukocytes: 10 [2 - 9] %; NPTST004-?GT: 29 [9 - 32] U/L; NPTST006-A/G: 1.07 [0.4 - 1.5] -; NPTST022-AMY: 69 [44 - 132] U/L; NPTST080-C-REACTIVE PROTEIN: 1.86 [0 - 0.14] MG/DL; NPTST085-C?: 106 [101 - 108] MMOL/L; NPTST133-CMV-AGC7: NEGATIVE [0 - NOT REPORTED] -; NPTST134-CMV-IGM: ?0.85 [NOT REPORTED - NOT REPORTED] -; NPTST135-CMV.G ANTIBODY CONCENTRATION: ??250.0 [0 - NOT REPORTED] -; NPTST181-EBNA?ANTIBODY: 20 [0 - NOT REPORTED] DOUBLE; NPTST185-EBV-ANTI VCA-IGG: 80 [0 - NOT REPORTED] DOUBLE; NPTST186-EBV-ANTI VCA-IGM: ?10 [0 - NOT REPORTED] DOUBLE; NPTST189-EGFR: 71.1 [90 - NOT REPORTED] mL/min/1.73m2; NPTST298-K: 3.0 [3.6 - 4.8] MMOL/L; NPTST320-MCH: 30.1 [27.5 - 33.2] PG; NPTST321-MCHC: 33.3 [31.7 - 35.3] G/DL; NPTST323-MCV: 90. [83.6 - 98.2] FL; NPTST341-MPV: 8.9 [7.4 - 10.4] FL; NPTST347-NA: 144 [138 - 145] MMOL/L; NPTST350-NEGATIVE CELL COUNT: 0 [NOT REPORTED - NOT REPORTED] -; NPTST384-PCT: 0.20 [0.115 - 0.2] %; NPTST385-PDW: 9.4 [NOT REPORTED - NOT REPORTED] %; NPTST413-PT: 11.7 [9.8 - 12.1] SEC; NPTST414-PT INR: 1.00 [0.8 - 1.2] -; NPTST415-PT%: 99.6 [70 - 130] %; NPTST424-RDW: 14 [11 - 14.3] %; NPTST449-SEG%: 61.0 [NOT REPORTED - NOT REPORTED] %; NPTST465-STAB%: 5.0 [NOT REPORTED - NOT REPORTED] %; NPTST466-STAB+SEG%: 66.0 [NOT REPORTED - NOT REPORTED] %; NPTST477-T-BIL: 0.4 [0.4 - 1.5] MG/DL; NPTST509-UN: 9 [8 - 20] MG/DL; Neutrophils: 4280 [0 - NOT REPORTED] /uL; Neutrophils/Leukocytes: 68.2 [49 - 60] %; Phosphate: 1.000835 [0.871695 - 1.48511] MMOL/L; Protein: 227000 [158000 - 348000] mL; Protein: 56 [66 - 81] G/L; Urate: 237.93884

[154.660246 - 327.165905] UMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 58): OTHER COVID-19 NPTST379-PCR: NEGATIVE-NEGATIVE

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	64 (13 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 6[redacted] 歳女性であり，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，ウイルス感染の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），元喫煙者（1 日 1 箱を 40 年間），鉄欠乏性貧血及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与51日後＊　　，被験者はウイルス感染を発現した。投与64日後＊　　，ウイルス感染は消失した。

本事象発現前の 投与から約2か月後＊，被験者は白血球減少症（非重篤）を発現した。

投与51日後＊　　，被験者のリンパ球数はさらに減少した（結果は提供されていない）。投与56日後＊　　，被験者は発熱し，病院を受診した。被験者は入院を勧められたが拒否し，オセルタミビル及びアセトアミノフェンの投与が開始された。投与58日後＊　　，被験者は発熱及び関節痛のため入院した。投与62日後＊　　，被験者のリンパ球数は増加し，体温は正常範囲内であ

った。投与64日後＊，被験者の症状は改善し，被験者は退院した。

治験責任医師によると，被験者は感染症に罹患しやすかった。

本事象により治験薬の投与は完全に中止された。

投与された薬剤は，オセルタミビルリン酸塩及び acetaminofen であった。

Causality for UPADACITINIB (Blinded)

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1) Viral infection (10047461) (Viral infection (10047461)) [v.23.0] [10047461]

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 VIRAL INFECTION

- Investigator: Not applicable

- AbbVie: Event is common in the general population particularly at this time of year.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABSOLUTE LYMPHOCYTE COUNT: 0.91 x10^3/ul (normal 0.80 to 3.00)

[redacted] 20[redacted] ABSOLUTE NEUTROPHIL COUNT: 6.70 x10^3/ul (normal 1.96 to 7.23)

[redacted] 20[redacted] ALBUMIN: 2.9 G/DL (normal 4.1 to 5.1)

[redacted] 20[redacted] **BACTERIA CELL COUNT:** 0

[redacted] 20[redacted] **BASOPHILS:** 0.5 % (normal 0 to 1)

[redacted] 20[redacted] **CMV-AGC7:** negative (low normal -0)

[redacted] 20[redacted] **CMV-IGM:** less than 0.85.

[redacted] 20[redacted] **CMV.G ANTIBODY CONCENTRATION:** 250.00 no units (normal >0)

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

[redacted] 20[redacted] **CREATININE KINASE:** 29 U/L (normal 41 to 53)

[redacted] 20[redacted] **CT SCAN:** No calcified granulomas, no pleural scarring or thickening, No signs of active TB, no findings indicative of previous TB infection, diffuse pale ground-glass opacity at lungs on CT (+)

[redacted] 20[redacted] **EBNA ANTIBODY:** 20 no units (normal >0)

[redacted] 20[redacted] **EBV-ANTI VCA-IGG:** 80 no units (normal >0)

[redacted] 20[redacted] **EBV-ANTI VCA-IGM:** less than 10.

[redacted] 20[redacted] **EOSINOPHILS:** 0.0 % (normal 2 to 5)

[redacted] 20[redacted] **HEMATOCRIT:** 37 % (normal 34 to 48)

[redacted] 20[redacted] **HEMATOCRIT:** 30.6 % (normal 35.1 to 44.4)

[redacted] 20[redacted] **HEMOGLOBIN:** 12.5 G/DL (normal 11.5 to 15.8)

[redacted] 20[redacted] **HEMOGLOBIN:** 10.2 G/DL (normal 11.6 to 14.8)

[redacted] 20[redacted] **K:** 3.0 MMOL/L (normal 3.6 to 4.8)

[redacted] 20[redacted] **LYMPHOCYTES:** 23.0 %

[redacted] 20[redacted] **LYMPHOCYTES:** 25.4 % (normal 32 to 43)

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 1590 ML

[redacted] 20[redacted] **NEUTROPHILS:** 68.2 % (normal 49 to 60)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 4280 ML

[redacted] 20[redacted] **PCR:** Covid-19 negative

[redacted] **20[redacted] PLATELET COUNT:** 281 x10^3/ul (normal 130 to 394)

[redacted] **20[redacted] PROTEIN:** 5.6 G/DL (normal 6.6 to 8.1)

[redacted] **20[redacted] RBC:** 3390000 ML (normal 3860000 to 4920000)

[redacted] **20[redacted] WBC:** 7.87 x10^3/ul (normal 3.80 to 10.70)

[redacted] **20[redacted] WBC:** 6270 ML (normal 3300 to 8600)

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
潰瘍性大腸炎	X	X		
横隔膜ヘルニア	X			

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo	5[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	19[redacted]
ULCERATIVE COLITIES	19[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	35	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo			[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -203
BUDESONIDE	2 mg	QD	Y-M: 20[redacted] / -104
MESALAZINE	4.8 g	QD	Y-M: 20[redacted] / -104
MESALAZINE	1 g	QD	Y-M: 20[redacted] / -103
PREDNISONE	20 mg	BID	Y-M: 20[redacted] / -96
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: BAG	BID	Y-M: 20[redacted] / -3
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19[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
MESALAZINE	4.8 g	QD	Y-M: 20[redacted] / -104	ONGOING
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 17	ONGOING
PHENOXYMETHYLPENICILLIN	1 g	QID	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 40
ALFENTANIL	0.5 mg	QD	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 41
METHYLPREDNISOLONE	20 mg	TID	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 41
PREDNISONE	20 mg	BID	Y-M: 20[redacted] / 42	ONGOING
MESALAZINE	1 g	QD	Y-M: 20[redacted] / 44	ONGOING
ONDANSETRON	8 mg	PRN	Y-M: 20[redacted] / 46	ONGOING

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

Event Description	WORSENING OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 32
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 40): NPTST159-CRP: 80 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 41): STOOL NPTST116-CLOSTRIDIUM: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 41): PLAIN ABDOMINAL RADIOGRAPHY: WALLTHICKENING IN TRANSVERSUM; SIGMOIDOSCOPY: MAYO 3 UP TO 70 CM

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING

Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	LAST WEEK,NAUSEA, REDUCED APPETITE, WEIGHT LOSS. FROM [redacted] VOMITING AND DIARRHEA CRP 80, LEUCOCYTES 12
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	DIAPHRAGMATIC HERNIA WITHOUT OBSTRUCTION OR GANGRENE
Preferred term	横隔膜ヘルニア
AE Onset Date / Rx Day	[redacted]20[redacted] / 45 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 45): NPTST159-CRP: 7 [NOT REPORTED - 5] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 45): X-RAY ABDOMEN: HEIGHT OF THE LEFT DIAPHRAGM, AND NO SIGNS OF ILEUS; [redacted]20[redacted] (RX DAY 48): CT ABDOMEN, PELVIS, THORAX: LARGE INTRATHORACALT DIAPRHAGMA HERNIE LEFT SIDE, WITH MULTIPLE INTESTINAL SEGMENTS.; GASTROSCOPY: VENTRICLE PARTIALLY LOCATED IN THE THORAX REGION ON THE LEFT SIDE

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はノルウェーの 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 0.5 箱を 35 年間）及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与32日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。

投与40日後＊　，被験者は下痢，悪心，食欲減退，体重減少及び臨床検査値異常があり入院した。S 状結腸鏡検査により，遠位横行結腸までの全範囲で浮腫性粘膜が確認された。被験者はステロイドを静脈内投与された。投与44日後＊　，被験者は退院した。退院時には，被験者は臨床的に改善し，便は固くなっていた。

投与された薬剤は，salofalk，ソル・メドロール，apocillin 及び prednisone であった。

The patient's past medications include:

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.23.0]　[10009901]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF UC

- Investigator: Common Cold

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CLOSTRIDIUM TEST (STOOL):** NEGATIVE

[redacted] **20[redacted] CRP:** 80 MG/L (normal 0 to 80)

[redacted] **20[redacted] LEUKOCYTES:** 12 no unit

[redacted] **20[redacted] PLAIN ABDOMINAL RADIOGRAPHY:** WALL THICKENING IN TRANSVERSUM

[redacted] **20[redacted] SIGMOIDOSCOPY:** MAYO 3 UP TO 70 CM

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はノルウェーの 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，閉塞や壊疽を伴わない横隔膜ヘルニアの事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 0.5 箱を 35 年間）及び元飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与45日後＊　，被験者は閉塞や壊疽を伴わない横隔膜ヘルニアを発現した。

投与45日後＊　，被験者は急性の悪心及び数回の嘔吐のため再入院した。被験者は「肺が圧迫されるような感じ，又は何かが食道を塞いでいるような感じ」と訴えた。被験者はいくつかの診断を受け，ヘルニアの手術を提案された。治験責任医師の意見によると，被験者は悪心及び嘔吐により栄養障害になり得る危険因子を持っていた。投与49日後＊　，被験者は退院した。

治験責任医師によると，治験薬の投与は潰瘍性大腸炎の悪化のため完全に中止された。

投与された薬剤は，ゾフランであった。

The patient's past medications include:

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Diaphragmatic hernia (10012713) (Diaphragmatic hernia (10012713)) [v.22.0] [10012713]

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 DIAPHRAGMATIC HERNIA WITHOUT OBSTRUCTION OR GANGRENE

- Investigator: UNKNOWN

- AbbVie: Mechanism of action does not support causal association. Most common causes are trauma, delayed presentation of congenital and iatrogenic.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 7 MG/L (normal <5)

[redacted] **20[redacted] CT ABDOMEN:** LARGE INTRATHORACALT DIAPRHAGMA HERNIA LEFT, SIDE, WITH MULTIPLE INTESTINAL SEGMENTS.

[redacted] **20[redacted] CT PELVIS:** LARGE INTRATHORACALT DIAPRHAGMA HERNIA LEFT, SIDE, WITH MULTIPLE INTESTINAL SEGMENTS.

[redacted] **20[redacted] CT THORAX:** LARGE INTRATHORACALT DIAPRHAGMA HERNIA LEFT, SIDE, WITH MULTIPLE INTESTINAL SEGMENTS.

[redacted] **20[redacted] GASTROSCOPY:** VENTRICLE PARTIALLY LOCATED IN THE THORAX REGION ON THE LEFT SIDE

[redacted] **20[redacted] X-RAY ABDOMEN:** HEIGHT OF THE LEFT DIAPHRAGM, AND NO SIGNS OF ILEUS

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo /P2:ABT-494 45 mg	6[redacted]	MALE	WHITE

Medical History	Onset Year
ASTHMA BRONCHIALE	20[redacted]
BENIGN HYPERPLASIA OF PROSTATE	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
VITILIGO	NOT REPORTED

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: HEMORRHOIDAL SURGERY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	10	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo			[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 70	14

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4 g	QID	Y-M: 20[redacted] / -297
BUDESONIDE	2 mg	QD	Y-M: 20[redacted] / -239
ESCHERICHIA COLI	1.000 OTHER: CAPSULE	QD	Y-M: 20[redacted] / -239
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -225
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -198
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / -207
VEDOLIZUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -147
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / -33
MIDAZOLAM	2.5 mg	OTHER: ONCE	Y-M: 20[redacted] / -16
PROPOFOL	120 mg	QD	Y-M: 20[redacted] / -16
SUFENTANIL	7.5 mg	OTHER: ONCE	Y-M: 20[redacted] / -16
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 OTHER: SACHET	OTHER: ONCE	Y-M: 20[redacted] / -17
FLUTICASONE	INHALATION OTHER: SPRAY	OTHER: ONCE A WEEK	Y: 20[redacted]
BECLOMETASONE;FORMOTEROL	2 OTHER: SPRAY INHALATION	BID	Y: 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
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / -207	ONGOING
PARACETAMOL;TRAMADOL	37.5/325 mg	PRN	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 40
MEPHENOXALONE	200 mg	PRN	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 47
PARACETAMOL;TRAMADOL	37.5/325 mg	PRN	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 57
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 57	ONGOING
RED BLOOD CELLS	2 OTHER: UNIT	OTHER: ONCE	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 57
FLUTICASONE	INHALATION OTHER: SPRAY	OTHER: ONCE A WEEK	Y: 20[redacted]	ONGOING

BECLOMETASONE;FORMOTEROL	2 OTHER: SPRAY INHALATION	BID	Y: 20[redacted]	ONGOING

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

Event Description	SEVERE ANEMIC SYNDROME
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 57
Age at AE Onset	6[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 57): Hemoglobin: 80 [140 - 180] G/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	57
Duration of AE	1 DAY
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	IRON DEFICIENCY ANEMIA DUE TO AKTIVE DISEASE MAYO 3
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	EXACERBATION OF THE ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 71 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	

SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:36
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はスロバキア共和国の 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，重度の貧血症候群の事象を発現した。関連する病歴は，元喫煙者（1 日 2 箱を 10 年間），潰瘍性大腸炎，痔の手術及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与57日後＊　，被験者は重度の貧血症候群を発現した。投与57日後＊　，重度の貧血症候群は消失した。

投与57日後＊　，被験者は重度の貧血による呼吸困難，脱力及び浮動性めまいを経験した。被験者は赤血球濃厚液の輸血を受けた。投与58日後＊　，被験者は退院した。

The patient's past medications include:

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

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

BUDENOFALK SPM REC for ULCERATIVE COLITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

MUTAFLOR for ULCERATIVE COLITIS ([redacted])

PREDNISON for ULCERATIVE COLITIS ([redacted])

INFLECTRA for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

ZALDIAR for ARTHRALGIA ([redacted])

DORSIFLEX for ARTHRALGIA ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Anemia (10002272) (Anaemia (10002034)) [v.22.1] [10002272]

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 SEVERE ANEMIC SYNDROME

- Investigator: Iron deficiency anemia due to active disease mayo 3.

- AbbVie: Event more likely related to pre-existing ulcerative colitis. Additionally, screening hemoglobin was low even before start of study drug.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **COLONOSCOPY:** No normal mucosa (pancolitis)

[redacted] **HEMATOCRIT:** 31 % (normal 37 to 51)

[redacted] **HEMATOCRIT:** 29 % (normal 37 to 51)

[redacted] **20[redacted] HEMATOCRIT:** 28 % (normal 37 to 51)

[redacted] **20[redacted] HEMATOCRIT:** 28 % (normal 37 to 51)

[redacted] **20[redacted] HEMATOCRIT:** 28 % (normal 37 to 51)

[redacted] **20[redacted] HEMATOCRIT:** 31 % (normal 37 to 51)

Unknown date HEMATOCRIT: 28 % (normal 37 to 51)

[redacted] **20[redacted] HEMOGLOBIN:** 9.9 G/DL (normal 12.5 to 17)

[redacted] **20[redacted] HEMOGLOBIN:** 8.8 G/DL (normal 12.5 to 17)

[redacted] **20[redacted] HEMOGLOBIN:** 8.7 G/DL (normal 12.5 to 17)

[redacted] **20[redacted] HEMOGLOBIN:** 8.5 G/DL (normal 12.5 to 17)

[redacted] **20[redacted] HEMOGLOBIN:** 8.4 G/DL (normal 12.5 to 17)

[redacted] **20[redacted] HEMOGLOBIN:** 9.8 G/DL (normal 12.5 to 17)

Unknown date HEMOGLOBIN: 8.4 G/DL (normal 12.5 to 17.0)

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
虫垂炎	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:ABT-494 45 mg	4[redacted]	MALE	WHITE

Medical History	Onset Year
DEPRESSION	20[redacted]
LEFT SIDED UC	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	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	CURRENT	5 SESSIONS	2	
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	More than 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494 45 mg	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
SULFASALAZINE	2 g	BID	Y-M: 20[redacted]
ALPRAZOLAM	0.25 mg	PRN	Y-M: 20[redacted]
FLUOXETINE	40 mg	QD	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
CYCLIZINE	10 mg	OTHER: STAT	Y-M: 20[redacted] / -1
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -15
PYRIDOXINE	25 mg	QD	Y-M: 20[redacted] / -15
MIDAZOLAM	1 mg	QD	Y-M: 20[redacted] / -5
PROPOFOL	3 mL	QD	Y-M: 20[redacted] / -5
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	TID	Y-M: 20[redacted] / -6

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / / RX Day	Stop Year-Month / / RX Day
MESALAZINE	2 g	BID	Y-M: 20[redacted]	ONGOING
ALPRAZOLAM	0.25 mg	PRN	Y-M: 20[redacted]	ONGOING
FLUOXETINE	40 mg	QD	Y-M: 20[redacted]	ONGOING
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	TID	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 48
MIDAZOLAM	1 mg	QD	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 48
PROPOFOL	3 mL	QD	Y-M: 20[redacted] / 48	Y-M: 20[redacted] / 48
AMOXICILLIN;CLAVULANIC ACID	1.2 g	TID	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 50
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	1000 mL	BID	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 50
DEXAMETHASONE	4 mg	OTHER: STAT	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
GRANISETRON	1 mg	OTHER: STAT	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
LORNOXICAM	8 mg	BID	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49

MIDAZOLAM	1 mg	OTHER: STAT	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
MORPHINE	7.5 mg	OTHER: STAT	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
PARACETAMOL	1 g	QID	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 50
PETHIDINE	100 mg	QID	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 50
PROPOFOL	180 mg	OTHER: STAT	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
ROCURONIUM	50 mg	OTHER: STAT	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
SUGAMMADEX	100 mg	OTHER: STAT	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49
ZOPICLONE	7.5 mg	QD	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 49

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] / 49

Age at AE Onset 4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 49): Chloride: 100 [101 - 109] MMOL/L; Hemoglobin: 128 [125 - 173] G/L; Leukocytes: 4.9 [4 - 11] 10^9/L; Sodium: 135 [136 - 146] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 49): APPENDICECTOMY: INFLAMMED APPENDIX REMOVED; CONTRASTED CT ABDOMEN: INFLAMMED APPENDIX

AE Stopped Rx Day 49

Duration of AE 1 DAY

Severity SEVERE

Relation to Study Drug by Investigator NO REASONABLE POSSIBILITY

Investigator Alternative Etiology RARE COMPLICATION OF COLONOSCOPY

Discontinued Study Drug Due to the Event NO

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

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は南アフリカの 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，急性虫垂炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 2 箱を 35 年間）及び元飲酒者（1 日 4 杯以上）であった。

Event 1 の臨床経過：

投与49日後＊　，被験者は急性虫垂炎を発現した。投与49日後＊　，急性虫垂炎は消失した。

投与48日後＊　，被験者は投与 8 週時の結腸内視鏡検査を受けた。この検査の忍容性は良好であり，即時の合併症は発現しなかった。投与49日後＊　の朝，被験者は腹痛を発症した。最初は腹痛は軽度で痙攣性であり，日中に悪化し，痛みは右腸骨窩に限局していた。被験者には悪心及び寒気もあった。投与49日後＊　，被験者は入院した。バイタルは安定しており，熱はなく，腹膜症であった。被験者は治験責任医師及び待機中の一般外科医によって診察された。被験者は鎮痛薬及び輸液の静脈内投与を受けた。腹部の造影 CT 検査が行われ，炎症を起こした虫垂が確認された。被験者は午後遅くに虫垂切除を受けた。投与50日後＊　，被験者は退院した。

投与された薬剤は，maxolon，オーグメンチン，ペチジン，perfalgan 及び xepo rapid であった。

The patient's past medications include:

BUDESONIDE ENEMA for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

SALAZOPYRINE for ULCERATIVE COLITIS ([redacted])

CYCLIZINE for NAUSEA ([redacted])

MULITVITAMIN for VIRAL URTI ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute appendicitis (10000677) (Appendicitis (10003011)) [v.24.0] [10000677]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE APPENDICITIS

- Investigator: RARE COMPLICATION OF COLONOSCOPY

- AbbVie: Event is a common complication in the general population, with a 10% lifetime occurrence.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **CHLORIDE:** 100 MMOL/L (normal 101 to 109)

[redacted] **CONTRASTED CT ABDOMEN:** INFLAMMED APPENDIX

[redacted] **HEMOGLOBIN:** 12.8 G/DL (normal 12.5 to 17.3)

[redacted] **SODIUM:** 135 MMOL/L (normal 136 to 146)

[redacted] **WHITE BLOOD CELLS:** 4.9 X10**9/L (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
アラニンアミノトランスフェラーゼ増加				X
アスパラギン酸アミノトランスフェラーゼ増加				X
蜂巣炎	X			X
潰瘍性大腸炎		X		
γ-グルタミルトランスフェラーゼ増加				X
ヘモグロビン減少				X

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo	4[redacted]	FEMALE	ASIAN

Medical History	Onset Year
ANEMIA	20[redacted]
ANXIETY	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
OCCASIONAL HEADACHE	20[redacted]
ULCERATIVE COLITIS	20[redacted]
UPPER RESPIRATORY TRACT INFECTION	20[redacted]
URTICARIA	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.1 PACK	10	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
Placebo			[redacted]20[redacted]/ 1	[redacted]20[redacted]/ 57	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
ALPRAZOLAM	0.5 mg	OTHER: HS	Y-M: 20[redacted]
AMBROXOL	30 mg	TID	Y-M: 20[redacted]/ -32
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted]/ -32
MESALAZINE	1500 mg	QID	Y-M: 20[redacted]/ -32
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]/ -32
HYOSCINE	20 mg	OTHER: STAT	Y-M: 20[redacted]/ -7
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	137.155 g	QD	Y-M: 20[redacted]/ -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ALPRAZOLAM	0.5 mg	OTHER: HS	Y-M: 20[redacted]	ONGOING
MESALAZINE	1500 mg	QID	Y-M: 20[redacted]/ -32	Y-M: 20[redacted]/ 199
HYOSCINE	20 mg	OTHER: STAT	Y-M: 20[redacted]/ -7	Y-M: 20[redacted]/ -7
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	137.155 g	QD	Y-M: 20[redacted]/ -7	Y-M: 20[redacted]/ -7
AMPICILLIN;SULBACTAM	1000 mg	OTHER: Q6H	Y-M: 20[redacted]/ 13	Y-M: 20[redacted]/ 21
TRAMADOL	100 mg	QD	Y-M: 20[redacted]/ 13	Y-M: 20[redacted]/ 14
MORPHINE	3 mg	OTHER: Q6HPRN	Y-M: 20[redacted]/ 14	Y-M: 20[redacted]/ 16
PARACETAMOL;TRAMADOL	362.5 mg	QID	Y-M: 20[redacted]/ 16	Y-M: 20[redacted]/ 42

VANCOMYCIN	1000 mg	OTHER: Q8H	Y-M: 20[redacted]/ 16	Y-M: 20[redacted]/ 21
DICLOFENAC	100 mg	OTHER: HS	Y-M: 20[redacted]/ 17	Y-M: 20[redacted]/ 22
FUSIDIC ACID	20 mg	PRN	Y-M: 20[redacted]/ 17	Y-M: 20[redacted]/ 18
IRON	100 mg	OTHER: ONCE	Y-M: 20[redacted]/ 17	Y-M: 20[redacted]/ 19
POVIDONE-IODINE	20 %	PRN	Y-M: 20[redacted]/ 18	Y-M: 20[redacted]/ 58
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted]/ 21	Y-M: 20[redacted]/ 78
CILASTATIN;IMIPENEM	500 mg	OTHER: Q6H	Y-M: 20[redacted]/ 21	Y-M: 20[redacted]/ 42
TEICOPLANIN	600 mg	QD	Y-M: 20[redacted]/ 21	Y-M: 20[redacted]/ 42
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	5 g	QD	Y-M: 20[redacted]/ 23	Y-M: 20[redacted]/ 44
DIPHENHYDRAMINE	30 mg	OTHER: ONCE	Y-M: 20[redacted]/ 23	Y-M: 20[redacted]/ 23
DIMETICONE	80 mg	OTHER: TIDPC	Y-M: 20[redacted]/ 38	Y-M: 20[redacted]/ 58
OXETACAINE	5 mg	OTHER: TIDAC	Y-M: 20[redacted]/ 38	Y-M: 20[redacted]/ 65
ENTEROCOCCUS FAECALIS	1 g	OTHER: TIDPC	Y-M: 20[redacted]/ 41	Y-M: 20[redacted]/ 64
LINEZOLID	600 mg	PRN	Y-M: 20[redacted]/ 42	Y-M: 20[redacted]/ 78
ACETYLCYSTEINE	600 mg	BID	Y-M: 20[redacted]/ 43	Y-M: 20[redacted]/ 49
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted]/ 43	Y-M: 20[redacted]/ 49
HYOSCINE	20 mg	OTHER: STAT	Y-M: 20[redacted]/ 52	Y-M: 20[redacted]/ 52
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	137.155 g	QD	Y-M: 20[redacted]/ 52	Y-M: 20[redacted]/ 52
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted]/ 57	Y-M: 20[redacted]/ 71
GLYCYRRHIZA GLABRA;PAPAVER SOMNIFERUM	5 mL	QID	Y-M: 20[redacted]/ 57	Y-M: 20[redacted]/ 71
AMBROXOL	30 mg	TID	Y-M: 20[redacted]/ 65	Y-M: 20[redacted]/ 71
FLUCONAZOLE	150 mg	QD	Y-M: 20[redacted]/ 65	Y-M: 20[redacted]/ 65
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]/ 200	ONGOING

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

Event Description	RIGHT ANKLE CELLULITIS
Preferred term	蜂巣炎
AE Onset Date / Rx Day	[redacted]20[redacted]/ 13
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted](RX DAY 13): NPTST277-HS-CRP: 4.61 [0.1 - 0.3] MG/DL; [redacted]20[redacted](RX DAY 16): Hemoglobin: 73 [80 - 160] G/L

Microbiology

[redacted]20[redacted](RX DAY 15): OTHER SKIN PUS RIGHT ANKLE SUBCUTANEOUS ABSCESS (AFTER ASPIRATION) NPTST052-BACTERIAL CULTURE: NEGATIVE-NO AEROBIC PATHOGEN

SAE Supplemental Procedure

[redacted]20[redacted](RX DAY 15): MUSCULOSKELETAL ULTRASOUND: COBBLESTONE APPEARANCE WITH SOME POWER DOPPLER SIGNAL AND FLUID ACCUMULATION AND SYNOVIAL HYPERTROPHY; [redacted]20[redacted](RX DAY 16): SONOGRAPHY FOR PERIPHERAL VESSEL: NO DVT WAS NOTED AT BILATERAL LOWER LIMBS; [redacted]20[redacted](RX DAY 19): MRI WITH/WITHOUT CONTRAST--LOWER EXTREMITIES: SOME FLUID FILLED LOBULATED THICK WALL LESION UNDERNEATH THE DISEASED SKIN, SUSPECT ASBCESS FORMATION. EXTENSIVE SOFT TISSUE SWELLING WITH HYPEREMIC CHANGES NOTED AT MEDIAL ANKLE, LOWER LEG TO FOOT, L IKELY SOFT TISSUE INFECTIONS PROCESS. CONSIDER CELLULITIS WITH ABSCESS FORMATION. NO DEFINITE OSTEOMYELITIS. NO DEFINITE SEPTIC ARTHRITIS OF ANKLE.; RIGHT ANKLE HISTOPATHOLOGY: SUPPURATIVE INFLAMMATION WITH MARKED NEUTROPHIL INFILTRATION, NECROSIS AND FOCAL ULCERATION. NO EVIDENT VASCULITIS IS SEEN. A FEW GRAM+ COCCI ARE HIGHLIGHTED BY GRAM STAIN IN THE INFLAMMATORY AREAS. N O DEFINITE PATHOGEN CAN BE IDENTIFIED BY PAS OR ACID-FAST STAIN. INFECTION IS MORE FAVORED. PLEASE CORRELATE WITH CLINICAL FINDINGS AND CULTURE RESULTS.; [redacted]20[redacted](RX DAY 21): ECG: NORMAL ECG; [redacted]20[redacted](RX DAY 39): ECG: NORMAL ECG

AE Stopped Rx Day	44
Duration of AE	32 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RIGHT ANKLE TENDERNESS AND SWELLING AND REDNESS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Anemia

Event Description	LOW HGB < 8 DL
Preferred term	ヘモグロビン減少
AE Onset Date / Rx Day	[redacted]20[redacted]/ 16
Age at AE Onset	4[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Rx Day	21
Duration of AE	6 DAYS
Severity	SEVERE

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

Event #3: Event of Interest - Hepatic Disorder

Event Description	ALANINE AMINOTRANSFERASE INCREASED
Preferred term	アラニンアミノトランスフェラーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 18
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	31
Duration of AE	14 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Event of Interest - Hepatic Disorder

Event Description	ASPARTATE AMINOTRANSFERASE INCREASED
Preferred term	アスパラギン酸アミノトランスフェラーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 18
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	31
Duration of AE	14 DAYS

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

Event #5: Event of Interest - Anemia

Event Description	LOW HGB <10 G/DL
Preferred term	ヘモグロビン減少
AE Onset Date / Rx Day	[redacted]20[redacted] / 22
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	24
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #6: Event of Interest - Hepatic Disorder

Event Description	GGT INCREASED
Preferred term	γ-グルタミルトランスフェラーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 44
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	115 (58 DAYS AFTER LAST TREATMENT)

Duration of AE	72 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #7: AE Leading to Discontinuation of Study Drug

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 282 (225 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:36
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は台湾の 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，右足首の蜂巣炎の事象を発現した。関連する病歴は，

潰瘍性大腸炎，元喫煙者（1 日 0.1 箱を 10 年間）及び非飲酒者であった。

Event 1 の臨床経過：

投与13日後＊　　，被験者は右足首の蜂巣炎を発現した。投与44日後＊　，右足首の蜂巣炎は消失した。

投与13日後＊　　，被験者は右足首の痛み，重度の腫脹及び発赤があり入院した。臨床検査及び画像による診断が行われ，被験者は蜂巣炎と診断された。投与44日後＊　，被験者は退院した。

投与された薬剤は，トラマール，モルヒネ，ultracet，バンコマイシン，votan，フシジン酸，better-iodine，チエナム，ザイボックス，タゴシッド，ビオフェルミン R，ザイザル，ジフェンヒドラミン塩酸塩，actein，ユナシン及び c.b. strong ointment であった。

The patient's past medications include:

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

Causality for ABT-494 (Blinded)

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1) Cellulitis (10007882) (Cellulitis (10007882)) [v.21.1] [10007882]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of RIGHT ANKLE CELLULITIS

- Investigator: Right ankle tenderness and swelling and redness

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BACTERIAL CULTURE OF SKIN PUS RIGHT ANKLE SUBCUTANEOUS ABSCESS (AFTER ASPIRATION):** NEGATIVE- No aerobic pathogen

[redacted] **20[redacted] CRP:** 4.61 mg/dL (normal 0.1 to 0.3)

[redacted] **20[redacted] ECG:** NORMAL

[redacted] **20[redacted] ECG:** NORMAL

[redacted] **20[redacted] HEMOGLOBIN:** 7.3 G/DL (normal 8 to 16)

[redacted] **20[redacted] MRI WITH/WITHOUT CONTRAST--LOWER EXTREMITIES:** SOME FLUID FILLED LOBULATED THICK WALL LESION UNDERNEATH THE DISEASED SKIN, SUSPECT ASBCESS FORMATION. EXTENSIVE SOFT TISSUE SWELLING WITH HYPEREMIC CHANGES NOTED AT MEDIAL ANKLE, LOWER LEG TO FOOT, LIKELY SOFT TISSUE INFECTIONS PROCESS. CONSIDER CELLULITIS WITH ABSCESS FORMATION. NO DEFINITE OSTEOMYELITIS. NO DEFINITE SEPTIC ARTHRITIS OF ANKLE.

[redacted] **20[redacted] MUSCULOSKELETAL ULTRASOUND:** COBBLESTONE APPEARANCE WITH SOME POWER DOPPLER SIGNAL AND FLUID ACCUMULATION AND SYNOVIAL HYPERTROPHY

[redacted] **20[redacted] RIGHT ANKLE HISTOPATHOLOGY:** SUPPURATIVE INFLAMMATION WITH MARKED NEUTROPHIL INFILTRATION, NECROSIS AND FOCAL ULCERATION. NO EVIDENT VASCULITIS IS SEEN. A FEW GRAM+ COCCI ARE HIGHLIGHTED BY GRAM STAIN IN THE INFLAMMATORY AREAS. NO DEFINITE PATHOGEN CAN BE IDENTIFIED BY PAS OR ACID-FAST STAIN. INFECTION IS MORE FAVORED. PLEASE CORRELATE WITH CLINICAL FINDINGS AND CULTURE RESULTS.

[redacted] **20[redacted] SONOGRAPHY FOR PERIPHERAL VESSEL:** NO DVT WAS NOTED AT BILATERAL LOWER LIMBS

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Alanine aminotransferase increased: Asymptomatic.
Aspartate aminotransferase increased: Asymptomatic. Attributed to use of new prescription or over the counter medications.

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
大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo	3[redacted]	MALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
2 CM HIATAL HERNIA	20[redacted]
ANEMIA	20[redacted]
CHEST PAIN	20[redacted]
ESOPHAGITIS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPERTENSION	20[redacted]
LOW MAGNESIUM LEVELS	20[redacted]
NAUSEA	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: ESOPHAGOGASTRODUODENOSCOPY	20[redacted]
PRIOR PROCEDURES: HIP SURGERY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	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	CURRENT	Less than 2 DRINKS

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SACCHAROMYCES BOULARDII	250.000 mg	QD	Y-M: 20[redacted]
BENAZEPRIL	40 mg	QD	Y-M: 20[redacted]/ -295
COLECALCIFEROL	1,000 IU	QD	Y-M: 20[redacted]/ -295
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]/ -295
MAGNESIUM	500 mg	QD	Y-M: 20[redacted]/ -295
OMEPRAZOLE	40 mg	BID	Y-M: 20[redacted]/ -295
SULFASALAZINE	500 mg	TID	Y-M: 20[redacted]/ -295
PREDNISONE	10 mg	QD	Y-M: 20[redacted]/ -237
METRONIDAZOLE	500 mg	QD	Y-M: 20[redacted]/ -193
AZATHIOPRINE	50 mg	TID	Y-M: 20[redacted]/ -161
IRON	324 mg	QD	Y-M: 20[redacted]/ -161
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]/ -161
MAGNESIUM SULFATE;POTASSIUM SULFATE;SODIUM SULFATE	180 mL	BID	Y-M: 20[redacted]/ -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BENAZEPRIL	40 mg	QD	Y-M: 20[redacted]/ -295	ONGOING
COLECALCIFEROL	1,000 IU	QD	Y-M: 20[redacted]/ -295	ONGOING
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]/ -295	ONGOING
MAGNESIUM	500 mg	QD	Y-M: 20[redacted]/ -295	ONGOING
OMEPRAZOLE	40 mg	BID	Y-M: 20[redacted]/ -295	ONGOING
SULFASALAZINE	500 mg	TID	Y-M: 20[redacted]/ -295	Y-M: 20[redacted]/ 12
IRON	324 mg	QD	Y-M: 20[redacted]/ -161	ONGOING
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]/ -161	Y-M: 20[redacted]/ 11

MAGNESIUM SULFATE;POTASSIUM SULFATE;SODIUM SULFATE	180 mL	BID	Y-M: 20[redacted]/ -7	Y-M: 20[redacted]/ -7
BACITRACIN;HYDROCORTISONE;NEOMYCIN;POLYMYXIN B	1 OTHER: PACKET	PRN	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 3
COLECALCIFEROL	1,000 OTHER: UNITS	QD	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 5
HYDROMORPHONE	0.5 mg	OTHER: Q2H PRN	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 5
IRON	325 mg	QD	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 3
LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS BULGARICUS	1 OTHER: TAB (UNKNOWN DOSE)	QD	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 3
MAGNESIUM OXIDE	400 mg	QD	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 3
METHYLPREDNISOLONE	125 mg	OTHER: Q8H	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 3
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 1
ONDANSETRON	8 mg	PRN	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 1
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 1
PIPERACILLIN;TAZOBACTAM	3.375 g	OTHER: Q8H	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 5
SODIUM CHLORIDE	1,000 mL	OTHER: Q6H40M	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 3
VANCOMYCIN	1 g	OTHER: Q8H	Y-M: 20[redacted]/ 1	Y-M: 20[redacted]/ 5
ALPRAZOLAM	1 mg	TID	Y-M: 20[redacted]/ 12	Y-M: 20[redacted]/ 25
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]/ 12	Y-M: 20[redacted]/ 18
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted]/ 12	Y-M: 20[redacted]/ 20
PREDNISONE	20 mg	QD	Y-M: 20[redacted]/ 12	Y-M: 20[redacted]/ 18
GLUCOSE;SODIUM CHLORIDE	1000 mL	OTHER: Q10H	Y-M: 20[redacted]/ 17	Y-M: 20[redacted]/ 20
HYDROMORPHONE	2 mg	PRN	Y-M: 20[redacted]/ 17	Y-M: 20[redacted]/ 20
LORAZEPAM	.5 mg	PRN	Y-M: 20[redacted]/ 17	Y-M: 20[redacted]/ 20
HYDROCODONE;PARACETAMOL	1 OTHER: TAB (NO UNITS PROVIDED ON MEDICATION FORM FROM HOSPITAL)	PRN	Y-M: 20[redacted]/ 18	Y-M: 20[redacted]/ 20
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted]/ 18	Y-M: 20[redacted]/ 20
PARACETAMOL	100 mL	PRN	Y-M: 20[redacted]/ 18	Y-M: 20[redacted]/ 20
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]/ 19	Y-M: 20[redacted]/ 20
BENAZEPRIL	40 mg	QD	Y-M: 20[redacted]/ 19	Y-M: 20[redacted]/ 20
COLECALCIFEROL	1000 IU	QD	Y-M: 20[redacted]/ 19	Y-M: 20[redacted]/ 20

HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]/ 19	Y-M: 20[redacted]/ 20
IRON	325 mg	QD	Y-M: 20[redacted]/ 19	Y-M: 20[redacted]/ 20
LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS BULGARICUS	1 OTHER: TAB (NO UNITS PROVIDED ON MEDICATION LIST)	QD	Y-M: 20[redacted]/ 19	Y-M: 20[redacted]/ 20
MAGNESIUM OXIDE	400 mg	QD	Y-M: 20[redacted]/ 19	Y-M: 20[redacted]/ 20
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]/ 19	Y-M: 20[redacted]/ 20
PREDNISONE	40 mg	QD	Y-M: 20[redacted]/ 19	Y-M: 20[redacted]/ 20
GLUCONATE SODIUM;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE	1000 mL	OTHER: Q6H40M	Y-M: 20[redacted]/ 24	Y-M: 20[redacted]/ 26
HYDROMORPHONE	1 mg	PRN	Y-M: 20[redacted]/ 24	Y-M: 20[redacted]/ 27
OXYCODONE	20 mg	PRN	Y-M: 20[redacted]/ 24	Y-M: 20[redacted]/ 28
PARACETAMOL	650 mL	PRN	Y-M: 20[redacted]/ 24	Y-M: 20[redacted]/ 32
POTASSIUM	100 mL	OTHER: Q1H	Y-M: 20[redacted]/ 24	ONGOING
LEVOFLOXACIN	100 mL	OTHER: Q24H	Y-M: 20[redacted]/ 25	Y-M: 20[redacted]/ 29
METHYLPREDNISOLONE	125 mg	OTHER: Q8H	Y-M: 20[redacted]/ 25	Y-M: 20[redacted]/ 28
METRONIDAZOLE;SODIUM CHLORIDE	100 mL	OTHER: Q8H	Y-M: 20[redacted]/ 25	Y-M: 20[redacted]/ 29
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]/ 26	Y-M: 20[redacted]/ 28
COLECALCIFEROL	1000 IU	QD	Y-M: 20[redacted]/ 26	Y-M: 20[redacted]/ 32
LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS BULGARICUS	1 OTHER: TAB (UNITS UNKNOWN ON HOSPITAL MEDICATION REPORT)	QD	Y-M: 20[redacted]/ 26	Y-M: 20[redacted]/ 32
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted]/ 26	Y-M: 20[redacted]/ 32
MAGNESIUM	500 mg	QD	Y-M: 20[redacted]/ 26	ONGOING
MAGNESIUM OXIDE	400 mg	BID	Y-M: 20[redacted]/ 26	Y-M: 20[redacted]/ 32
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]/ 26	Y-M: 20[redacted]/ 32
SODIUM CHLORIDE	1000 mL	OTHER: Q20H	Y-M: 20[redacted]/ 26	Y-M: 20[redacted]/ 32
HYDROMORPHONE	0.5 mg	PRN	Y-M: 20[redacted]/ 27	Y-M: 20[redacted]/ 32
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]/ 28	Y-M: 20[redacted]/ 32
METFORMIN	500 mg	BID	Y-M: 20[redacted]/ 28	Y-M: 20[redacted]/ 32
METHYLPREDNISOLONE	100 mg	QD	Y-M: 20[redacted]/ 28	Y-M: 20[redacted]/ 30
OXYCODONE	20 mg	QD	Y-M: 20[redacted]/ 28	Y-M: 20[redacted]/ 29

PREDNISONE	40 mg	QD	Y-M: 20[redacted]/ 28	Y-M: 20[redacted]/ 30
SODIUM CHLORIDE	250 mL	PRN	Y-M: 20[redacted]/ 28	Y-M: 20[redacted]/ 32
OXYCODONE	20 mg	QD	Y-M: 20[redacted]/ 29	Y-M: 20[redacted]/ 32
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted]/ 30	Y-M: 20[redacted]/ 32
METHYLPREDNISOLONE	125 mg	OTHER: Q8HR	Y-M: 20[redacted]/ 30	Y-M: 20[redacted]/ 32

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

Event Description	DIFFUSE COLITIS
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 1
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted](RX DAY 1): Alanine Aminotransferase: 19 [5 - 55] U/L; Albumin: 29 [35 - 50] G/L; Alkaline Phosphatase: 131 [40 - 150] U/L; Aspartate Aminotransferase: 23 [5 - 34] U/L; Basophils: 0 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0 [0 - 2] %; Bilirubin: 10.262334 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 7.49637 [3.21273 - 9.28122] MMOL/L; Calcium: 2.270541 [2.095884 - 2.545002] MMOL/L; Chloride: 89 [98 - 107] MMOL/L; Creatinine: 160.893933 [63.650347 - 110.504075] UMOL/L; Eosinophils: 0.22 [0 - 1.08] 10^9/L; Eosinophils/Leukocytes: 2 [0 - 10] %; Erythrocytes: 5.38 [4.6 - 5.9] 10^12/L; Glucose: 7.715473 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.349 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 109 [135 - 175] G/L; Leukocytes: 10.78 [4.8 - 10.8] 10^9/L; Lymphocytes: 1.62 [0.96 - 4.32] 10^9/L; Lymphocytes/Leukocytes: 15 [20 - 40] %; Monocytes: 1.94 [0 - 1.62] 10^9/L; Monocytes/Leukocytes: 18 [0 - 15] %; NPTST023-AMYLASE: 104 [25 - 125] U/L; NPTST028-ANION GAP: 12 [5 - 15] MMOL/L; NPTST039-APTT: 27.5 [26.4 - 36.1] SEC; NPTST056-BAND NEUTROPHILS: 4 [0 - 8] %; NPTST078-C REACTIVE PROTEIN HIGH SENS: 24.196 [0 - 0.5] MG/DL; NPTST096-CARBON DIOXIDE: 25 [22 - 29] MMOL/L; NPTST150-CORRECTED CALCIUM: 10.0 [8.4 - 10.2] MG/DL; NPTST296-INR: 1.31 [0.88 - 1.13] SEC; NPTST303-LACTIC ACID: 1.1 [0.5 - 2] MMOL/L; NPTST316-LIPASE: 41 [8 - 78] U/L; NPTST324-MEAN CELL HEMOGLOBIN: 20.3 [27 - 33] PG; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 31.2 [31 - 36] G/DL; NPTST329-MEAN CORPUSCULAR VOLUME: 64.9 [80 - 100] FL; NPTST402-PROCALCITONIN: 0.59 [0 - 0.5] NG/ML; NPTST413-PT: 14.8 [9.7 - 12.3] SEC; NPTST428-RED BLOOD CELL DISTRIBUTION: 15.6 [11.5 - 14.5] %; NPTST448-SEG NEUTTROPHILS # MANUAL: 6.58 [2.4 - 8.1] 10^3/UL; Neutrophils: 7.01 [2.4 - 8.1] 10^9/L; Neutrophils/Leukocytes: 61 [50 - 75] %; Platelets: 100 [130 - 400] 10^9/L; Potassium: 3 [3.5 - 5.1] MMOL/L; Protein: 80 [64 - 83] G/L; Sodium: 126 [136 - 145] MMOL/L; Specific Gravity: 1.040 [1.005 - 1.035] UNIT NOT REPORTED; pH: 5.0 [4.6 - 8] UNIT NOT REPORTED; [redacted]20[redacted](RX DAY 2): Blood Urea Nitrogen: 5.35455 [3.21273 - 9.28122] MMOL/L; Calcium: 2.145786 [2.095884 - 2.545002] MMOL/L; Chloride: 96 [98 - 107] MMOL/L; Creatinine: 98.127619 [63.650347 - 110.504075] UMOL/L; Glucose: 8.714599 [3.88549 - 5.5507] MMOL/L; NPTST028-ANION GAP: 10 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 24 [22 - 29] MMOL/L; Potassium: 3.4 [3.5 - 5.1] MMOL/L; Sodium: 130 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 3): Basophils: 0.04 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 2] %; Creatinine: 78.678901 [63.650347 - 110.504075] UMOL/L; Eosinophils/Leukocytes: 0 [0 - 10] %; Erythrocytes: 4.47 [4.6 - 5.9] 10^12/L; Hematocrit: 0.287 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 92 [135 - 175] G/L; Leukocytes: 12.58 [4.8 - 10.8] 10^9/L; Lymphocytes: 1.33 [0.96 - 4.32] 10^9/L; Lymphocytes/Leukocytes: 10.6 [20 - 40] %; Monocytes: 0.74 [0 - 1.62] 10^9/L; Monocytes/Leukocytes: 5.9 [0 - 15] %; NPTST078-C REACTIVE PROTEIN HIGH SENS: 20.064 [0 - 0.5] MG/DL; NPTST287-IMMATURE GRAN #: 0.47 [0.01 - 0.03] 10^3/UL; NPTST289-IMMATURE GRAN %: 3.70 [0.1 - 0.5] %; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 32.1 [31 - 36] G/DL; NPTST326-MEAN CORPUSCULAR HEMOGLOBIN: 20.6 [27 - 33] PG; NPTST329-MEAN CORPUSCULAR VOLUME: 64.2 [80 - 100] FL; NPTST428-RED BLOOD CELL DISTRIBUTION: 15.8 [11.5 - 14.5] %; NPTST521-VANCOMYCIN TROUGH: 12.1 [10 - 20]

UG/ML; Neutrophils: 10 [2.4 - 8.1] 10^9/L; Neutrophils/Leukocytes: 79.5 [50 - 75] %; Platelets: 116 [130 - 400] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted](RX DAY 1): CT ABDOMINAL PELVIS: DIFFUSE COLITIS

AE Stopped Rx Day	5 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COMBINATION OF ULCERATIVE COLITIS DIAGNOSIS AND COLONOSCOPY. MAY HAVE INDUCED A FLARE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	DIFFUSE COLITIS
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted]/ 7 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted](RX DAY -23): Hemoglobin: 93 [135 - 175] G/L; [redacted]20[redacted](RX DAY 7): Alanine Aminotransferase: 45 [5 - 55] U/L; Albumin: 25 [35 - 50] G/L; Alkaline Phosphatase: 143 [40 - 150] U/L; Aspartate Aminotransferase: 29 [5 - 34] U/L; Basophils: 0 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0 [0 - 2] %; Bilirubin: 13.683112 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 2.85576 [3.21273 - 9.28122] MMOL/L; Calcium: 2.220639 [2.095884 - 2.545002] MMOL/L; Chloride: 95 [98 - 107] MMOL/L; Creatinine: 97.243586 [63.650347 - 110.504075] UMOL/L; Eosinophils: 0 [0 - 1.08] 10^9/L; Eosinophils/Leukocytes: 0 [0 - 10] %; Erythrocytes: 5.43 [4.6 - 5.9] 10^12/L; Glucose: 5.828235 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.363 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 110 [135 - 175] G/L; Leukocytes: 12.76 [4.8 - 10.8] 10^9/L; Lymphocytes: 2.81 [0.96 - 4.32] 10^9/L; Lymphocytes/Leukocytes: 19 [20 - 40] %; Monocytes: 0.67 [0 - 1.62] 10^9/L; Monocytes/Leukocytes: 5 [0 - 15] %; NPTST028-ANION GAP: 10 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 30 [22 - 29] MMOL/L; NPTST303-LACTIC ACID: 1.5 [0.5 - 2] MMOL/L; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 30.3 [31 - 36] G/DL; NPTST326-MEAN CORPUSCULAR HEMOGLOBIN: 20.3 [27 - 33] PG; NPTST329-MEAN CORPUSCULAR VOLUME: 66.9 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 9.7 [8.8 - 12.4] FL; NPTST402-PROCALCITONIN: 0.25 [0 - 0.5] NG/ML; NPTST429-RED BLOOD CELL DISTRIBUTION WID: 16.7 [11.5 - 14.5] %; NPTST447-SEG NEUTROPHILS # MAN: 8.68 [2.4 - 8.1] 10^3/UL; Neutrophils: 8.94 [2.4 - 8.1] 10^9/L; Neutrophils/Leukocytes: 68 [50 - 75] %; Platelets: 309 [130 - 400] 10^9/L; Potassium: 3 [3.5 - 5.1] MMOL/L; Protein: 66 [64 - 83] G/L; Sodium: 135 [136 - 145] MMOL/L; Specific Gravity: 1.010 [1.005 - 1.035] UNIT NOT REPORTED; pH: 5.0 [4.6 - 8] UNIT NOT REPORTED; [redacted]20[redacted](RX DAY 8): Alanine Aminotransferase: 36 [5 - 55] U/L; Albumin: 21 [35 - 50] G/L; Alkaline Phosphatase: 120 [40 - 150] U/L; Aspartate Aminotransferase: 21 [5 - 34] U/L; Bilirubin: 6.841556 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 3.5697 [3.21273 - 9.28122] MMOL/L; Calcium: 1.99608 [2.095884 - 2.545002] MMOL/L; Chloride: 99 [98 - 107] MMOL/L; Creatinine: 78.678901 [63.650347 - 110.504075] UMOL/L; Erythrocytes: 4.62 [4.6 - 5.9] 10^12/L; Glucose: 12.045019 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.311 [0.41 - 0.51] FRACTION OF 1; Leukocytes: 10.37 [4.8 - 10.8] 10^9/L;

NPTST028-ANION GAP: 7 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 26 [22 - 29] MMOL/L; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 29.9 [31 - 36] G/DL; NPTST326-MEAN CORPUSCULAR HEMOGLOBIN: 20.1 [27 - 33] PG; NPTST329-MEAN CORPUSCULAR VOLUME: 67.3 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 10.2 [8.8 - 12.4] FL; NPTST429-RED BLOOD CELL DISTRIBUTION WID: 16.4 [11.5 - 14.5] %; Platelets: 257 [130 - 400] 10^9/L; Potassium: 4 [3.5 - 5.1] MMOL/L; Protein: 58 [64 - 83] G/L; Sodium: 132 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 9): Alanine Aminotransferase: 28 [5 - 55] U/L; Albumin: 21 [35 - 50] G/L; Alkaline Phosphatase: 107 [40 - 150] U/L; Aspartate Aminotransferase: 12 [5 - 34] U/L; Bilirubin: 5.131167 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 4.64061 [3.21273 - 9.28122] MMOL/L; Calcium: 2.045982 [2.095884 - 2.545002] MMOL/L; Chloride: 104 [98 - 107] MMOL/L; Creatinine: 71.606641 [63.650347 - 110.504075] UMOL/L; Erythrocytes: 4.28 [4.6 - 5.9] 10^12/L; Glucose: 10.490823 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.294 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 88 [135 - 175] G/L; Leukocytes: 14.83 [4.8 - 10.8] 10^9/L; NPTST028-ANION GAP: 8 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 24 [22 - 29] MMOL/L; NPTST319-MAGNESIUM: 1.7 [1.6 - 2.6] MG/DL; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 29.9 [31 - 36] G/DL; NPTST328-MEAN CORPUSCULAR HEMOGOBIN: 20.6 [27 - 33] PG; NPTST329-MEAN CORPUSCULAR VOLUME: 68.7 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 11.0 [8.8 - 12.4] FL; NPTST429-RED BLOOD CELL DISTRIBUTION WID: 16.3 [11.54 - 14.5] %; Platelets: 303 [130 - 400] 10^9/L; Potassium: 4.2 [3.5 - 5.1] MMOL/L; Protein: 56 [64 - 83] G/L; Sodium: 136 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 10): Alanine Aminotransferase: 25 [5 - 55] U/L; Albumin: 23 [35 - 50] G/L; Alkaline Phosphatase: 116 [40 - 150] U/L; Aspartate Aminotransferase: 9 [5 - 34] U/L; Bilirubin: 5.131167 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 4.64061 [3.21273 - 9.28122] MMOL/L; Calcium: 2.145786 [2.095884 - 2.545002] MMOL/L; Chloride: 104 [98 - 107] MMOL/L; Creatinine: 74.258738 [63.650347 - 110.504075] UMOL/L; Erythrocytes: 4.76 [4.6 - 5.9] 10^12/L; Glucose: 14.43182 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.326 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 96 [135 - 175] G/L; Leukocytes: 16.2 [4.8 - 10.8] 10^9/L; NPTST028-ANION GAP: 8 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 26 [22 - 29] MMOL/L; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 29.4 [31 - 36] G/DL; NPTST326-MEAN CORPUSCULAR HEMOGLOBIN: 20.0 [27 - 33] PG; NPTST329-MEAN CORPUSCULAR VOLUME: 68.5 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 10.1 [8.8 - 12.4] FL; NPTST429-RED BLOOD CELL DISTRIBUTION WID: 16.6 [11.5 - 14.5] %; Platelets: 328 [130 - 400] 10^9/L; Potassium: 4.3 [3.5 - 5.1] MMOL/L; Protein: 60 [64 - 84] G/L; Sodium: 138 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 12): Alanine Aminotransferase: 25 [5 - 55] U/L; Albumin: 21 [35 - 50] G/L; Alkaline Phosphatase: 96 [40 - 150] U/L; Aspartate Aminotransferase: 15 [5 - 34] U/L; Bilirubin: 5.131167 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 3.21273 [3.21273 - 9.28122] MMOL/L; Calcium: 2.021031 [2.095884 - 2.545002] MMOL/L; Chloride: 104 [98 - 107] MMOL/L; Creatinine: 76.910836 [63.650347 - 110.504075] UMOL/L; Erythrocytes: 4.57 [4.6 - 5.9] 10^12/L; Glucose: 10.379809 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.316 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 93 [135 - 175] G/L; Leukocytes: 14.45 [4.8 - 10.8] 10^9/L; NPTST001-% SATURATION: 8 [20 - 50] %; NPTST028-ANION GAP: 8 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 26 [22 - 29] MMOL/L; NPTST219-FERRITIN: 36 [21.8 - 274.6] NG/ML; NPTST297-IRON: 17 [65 - 175] UG/DL; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 29.4 [31 - 36] G/DL; NPTST326-MEAN CORPUSCULAR HEMOGLOBIN: 20.4 [27 - 33] PG; NPTST329-MEAN CORPUSCULAR VOLUME: 69.1 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 10.4 [8.8 - 12.4] FL; NPTST429-RED BLOOD CELL DISTRIBUTION WID: 17.3 [11.5 - 14.5] %; NPTST488-TOTAL IRON BINDING CAPACITY: 216 [171 - 564] UG/DL; NPTST494-TRANSFERRIN: 154 [174 - 364] MG/DL; Platelets: 320 [130 - 400] 10^9/L; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Protein: 51 [64 - 83] G/L; Sodium: 138 [136 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted](RX DAY 7): CT SCAN: CT SHOWS WALL THICKENING THROUGHOUT COLON WITH SURROUNDING INFLAMMATORY CHANGE CONSISTENT WITH INFECTIOUS VS INFLAMMATORY COLITIS, PHERINEPHRIC STRANDING AND STRANDING IN RETROPERITONEUM INCREASED COM PLARED TO PRIOR STUDY, APPENDIX IS DILATED WITH SURROUNDING INFLAMMATORY CHANGES SIMILAR TO PREVIOUS STUDY

AE Stopped Rx Day	12 (11 DAYS AFTER LAST TREATMENT)
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	IT IS LIKELY THAT THE COLONOSCOPY INDUCED A FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	DIFFUSE COLITIS
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted]/ 17 (16 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted](RX DAY 17): Alanine Aminotransferase: 19 [5 - 55] U/L; Albumin: 27 [35 - 50] G/L; Alkaline Phosphatase: 102 [40 - 150] U/L; Aspartate Aminotransferase: 12 [5 - 34] U/L; Basophils: 0.01 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0.1 [0 - 2] %; Bilirubin: 10.262334 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 2.85576 [3.21273 - 9.28122] MMOL/L; Calcium: 2.195688 [2.095884 - 2.545002] MMOL/L; Chloride: 98 [98 - 107] MMOL/L; Creatinine: 74.258738 [63.650347 - 110.504075] UMOL/L; Eosinophils: 0.03 [0 - 1.08] 10^9/L; Eosinophils/Leukocytes: 0.3 [0 - 10] %; Erythrocytes: 4.58 [4.6 - 5.9] 10^12/L; Glucose: 7.326924 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.315 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 94 [135 - 175] G/L; Leukocytes: 8.64 [4.8 - 10.8] 10^9/L; Lymphocytes: 1.5 [0.96 - 4.32] 10^9/L; Lymphocytes/Leukocytes: 17.4 [20 - 40] %; Monocytes: 0.9 [0 - 1.62] 10^9/L; Monocytes/Leukocytes: 10.4 [0 - 15] %; NPTST028-ANION GAP: 8 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 29 [22 - 29] MMOL/L; NPTST288-IMMATURE GRAN # (AUTO): 0.06 [0.01 - 0.03] 10^3/UL; NPTST290-IMMATURE GRAN % (AUTO): 0.70 [0.1 - 0.5] %; NPTST324-MEAN CELL HEMOGLOBIN: 20.5 [27 - 33] PG; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 29.8 [31 - 36] G/DL; NPTST329-MEAN CORPUSCULAR VOLUME: 68.8 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 9.5 [8.8 - 12.4] FL; NPTST429-RED BLOOD CELL DISTRIBUTION WID: 18.2 [11.5 - 14.5] %; Neutrophils: 6.14 [2.4 - 8.1] 10^9/L; Neutrophils/Leukocytes: 71.1 [50 - 75] %; Platelets: 133 [130 - 400] 10^9/L; Potassium: 3.6 [3.5 - 5.1] MMOL/L; Protein: 67 [64 - 83] G/L; Sodium: 135 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 18): Specific Gravity: 1.021 [1.005 - 1.035] UNIT NOT REPORTED; pH: 5.0 [4.6 - 8] UNIT NOT REPORTED; [redacted]20[redacted](RX DAY 19): NPTST304-LACTIC ACIDS: 1.2 [0.5 - 2] MMOL/L; NPTST402-PROCALCITONIN: 0.35 [0 - 0.5] NG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted](RX DAY 17): CT ABD PELVIS: REDEMONSTRATION OF DIFFUSE COLITIS WITH SOME IMPROVEMENT FROM THE PRIOR STUDY

AE Stopped Rx Day	20 (19 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	PATIENT WAS EXPERIENCING A FLARE DUE TO UC DIAGNOSIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #4: Serious Adverse Event

Event Description	DIFFUSE COLITIS
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted]/ 24 (23 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted](RX DAY -2): Leukocytes: 15.25 [4.8 - 10.8] 10^9/L; [redacted]20[redacted](RX DAY 24): Alanine Aminotransferase: 19 [5 - 55] U/L; Albumin: 22 [35 - 50] G/L; Alkaline Phosphatase: 134 [40 - 150] U/L; Aspartate Aminotransferase: 23 [5 - 34] U/L; Bilirubin: 17.10389 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 4.99758 [3.21273 - 9.28122] MMOL/L; Calcium: 2.095884 [2.095884 - 2.545002] MMOL/L; Chloride: 91 [98 - 107] MMOL/L; Creatinine: 145.865379 [63.650347 - 110.504075] UMOL/L; Erythrocytes: 4.54 [4.6 - 5.9] 10^12/L; Glucose: 7.049389 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.302 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 92 [135 - 175] G/L; Leukocytes: 10.41 [4.8 - 10.8] 10^9/L; NPTST028-ANION GAP: 12 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 28 [22 - 29] MMOL/L; NPTST303-LACTIC ACID: 8.4 [0.5 - 2] MMOL/L; NPTST319-MAGNESIUM: 1.7 [1.6 - 2.6] MG/DL; NPTST324-MEAN CELL HEMOGLOBIN: 20.3 [27 - 33] PG; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 30.5 [31 - 36] G/DL; NPTST329-MEAN CORPUSCULAR VOLUME: 66.5 [80 - 100] FL; NPTST402-PROCALCITONIN: 0.63 [0 - 0.5] NG/ML; NPTST431-RED CELL DISTRIBUTION WIDTH: 17.0 [11.5 - 14.5] %; Platelets: 103 [130 - 400] 10^9/L; Potassium: 2.7 [3.5 - 5.1] MMOL/L; Protein: 70 [64 - 83] G/L; Sodium: 131 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 25): Basophils: 0.1 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0 [0 - 2] %; Blood Urea Nitrogen: 5.71152 [3.21273 - 9.28122] MMOL/L; Calcium: 1.971129 [2.095884 - 2.545002] MMOL/L; Chloride: 94 [98 - 107] MMOL/L; Creatinine: 129.06876 [63.650347 - 110.504075] UMOL/L; Eosinophils: 0 [0 - 1.08] 10^9/L; Eosinophils/Leukocytes: 0 [0 - 10] %; Erythrocytes: 3.88 [4.6 - 5.9] 10^12/L; Glucose: 5.828235 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.277 [0.41 - 0.51] FRACTION OF 1; Hematocrit: 0.263 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 85 [135 - 175] G/L; Hemoglobin: 78 [135 - 175] G/L; Leukocytes: 9.88 [4.8 - 10.8] 10^9/L; Lymphocytes: 1.48 [0.96 - 4.32] 10^9/L; Lymphocytes/Leukocytes: 15 [20 - 40] %; Monocytes: 0.3 [0 - 1.62] 10^9/L; Monocytes/Leukocytes: 3 [0 - 15] %; NPTST028-ANION GAP: 10 [5 - 15] MMOL/L; NPTST057-BAND NEUTROPHILS %: 11 [0 - 8] %; NPTST096-CARBON DIOXIDE: 26 [22 - 29] MMOL/L; NPTST319-MAGNESIUM: 1.5 [1.6 - 2.6] MG/DL; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 29.7 [31 - 36] G/DL; NPTST326-MEAN CORPUSCULAR HEMOGLOBIN: 20.1 [27 - 33] PG; NPTST329-MEAN CORPUSCULAR VOLUME: 67.8 [80 - 100] FL; NPTST431-RED CELL DISTRIBUTION WIDTH: 16.8 [11.5 - 14.5] %; Neutrophils: 7.12 [2.4 - 8.1] 10^9/L; Neutrophils/Leukocytes: 61 [50 - 75] %; Platelets: 72 [130 - 400] 10^9/L; Potassium: 3.2 [3.5 - 5.1] MMOL/L; Sodium: 130 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 26): Alanine Aminotransferase: 17 [5 - 55] U/L; Albumin: 19 [35 - 50] G/L; Alkaline Phosphatase: 114 [40 - 150] U/L; Aspartate Aminotransferase: 18 [5 - 34] U/L; Bilirubin: 5.131167 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 5.71152 [3.21273 - 9.28122] MMOL/L; Calcium: 2.145786 [2.095884 - 2.545002] MMOL/L; Chloride: 99 [98 - 107] MMOL/L; Creatinine: 72.490673 [63.650347 - 110.504075] UMOL/L; Erythrocytes: 3.73 [4.6 - 5.9] 10^12/L; Glucose: 11.434442 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.245 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 76 [135 - 175] G/L; Leukocytes: 8.82 [4.8 - 10.8] 10^9/L; NPTST028-ANION GAP: 9 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 24 [22 - 29] MMOL/L; NPTST324-MEAN CELL HEMOGLOBIN: 20.4 [27 - 33] PG; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 30.0 [31 - 36] G/DL; NPTST329-MEAN CORPUSCULAR VOLUME: 65.7 [80 - 100] FL; NPTST431-RED CELL DISTRIBUTION WIDTH: 16.8 [11.5 - 14.5] %; Platelets: 102 [130 - 400] 10^9/L; Potassium: 4.3 [3.5 - 5.1] MMOL/L; Protein: 64 [64 - 83] G/L; Sodium: 132 [136 - 145]

MMOL/L; [redacted]20[redacted](RX DAY 27): Alanine Aminotransferase: 15 [5 - 55] U/L; Albumin: 19 [35 - 50] G/L; Alkaline Phosphatase: 115 [40 - 150] U/L; Aspartate Aminotransferase: 15 [5 - 34] U/L; Bilirubin: 5.131167 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 5.35455 [3.21273 - 9.28122] MMOL/L; Calcium: 2.170737 [2.095884 - 2.545002] MMOL/L; Chloride: 103 [98 - 107] MMOL/L; Creatinine: 69.838575 [63.650347 - 110.504075] UMOL/L; Erythrocytes: 3.65 [4.6 - 5.9] 10^12/L; Glucose: 12.045019 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.245 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 74 [135 - 175] G/L; Leukocytes: 12.8 [4.8 - 10.8] 10^9/L; NPTST028-ANION GAP: 9 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 23 [22 - 29] MMOL/L; NPTST319-MAGNESIUM: 1.5 [1.6 - 2.6] MG/DL; NPTST324-MEAN CELL HEMOGLOBIN: 20.3 [27 - 33] PG; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 30.2 [31 - 36] G/DL; NPTST329-MEAN CORPUSCULAR VOLUME: 67.1 [80 - 100] FL; NPTST431-RED CELL DISTRIBUTION WIDTH: 16.8 [11.5 - 14.5] %; Platelets: 217 [130 - 400] 10^9/L; Potassium: 4.4 [3.5 - 5.1] MMOL/L; Protein: 59 [64 - 83] G/L; Sodium: 135 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 28): Alanine Aminotransferase: 15 [5 - 55] U/L; Albumin: 20 [35 - 50] G/L; Alkaline Phosphatase: 119 [40 - 150] U/L; Aspartate Aminotransferase: 13 [5 - 34] U/L; Bilirubin: 5.131167 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 4.64061 [3.21273 - 9.28122] MMOL/L; Calcium: 2.170737 [2.095884 - 2.545002] MMOL/L; Chloride: 103 [98 - 107] MMOL/L; Creatinine: 78.678901 [63.650347 - 110.504075] UMOL/L; Erythrocytes: 3.68 [4.6 - 5.9] 10^12/L; Glucose: 17.76224 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.247 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 76 [135 - 175] G/L; Leukocytes: 14.09 [4.8 - 10.8] 10^9/L; NPTST028-ANION GAP: 8 [5 - 15] MMOL/L; NPTST096-CARBON DIOXIDE: 24 [22 - 29] MMOL/L; NPTST319-MAGNESIUM: 1.4 [1.6 - 2.6] MG/DL; NPTST324-MEAN CELL HEMOGLOBIN: 20.7 [27 - 33] PG; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 30.8 [31 - 36] G/DL; NPTST329-MEAN CORPUSCULAR VOLUME: 67.1 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 11.4 [8.8 - 12.4] FL; NPTST431-RED CELL DISTRIBUTION WIDTH: 17.2 [11.5 - 14.5] %; NPTST528-WHOLE BLOOD GLUCOSE: 265 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 224 [70 - 100] MG/DL; Platelets: 296 [130 - 400] 10^9/L; Potassium: 4.5 [3.5 - 5.1] MMOL/L; Protein: 58 [64 - 83] G/L; Sodium: 135 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 29): Erythrocytes: 4.44 [4.6 - 5.9] 10^12/L; Hematocrit: 0.312 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 94 [135 - 175] G/L; Leukocytes: 30.1 [31 - 36] 10^9/L; Leukocytes: 13.62 [4.8 - 10.8] 10^9/L; NPTST324-MEAN CELL HEMOGLOBIN: 21.2 [27 - 33] PG; NPTST329-MEAN CORPUSCULAR VOLUME: 70.3 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 10.0 [8.8 - 12.4] FL; NPTST431-RED CELL DISTRIBUTION WIDTH: 19.5 [11.5 - 14.5] %; NPTST528-WHOLE BLOOD GLUCOSE: 157 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 151 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 99 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 218 [70 - 100] MG/DL; Platelets: 348 [130 - 400] 10^9/L; [redacted]20[redacted](RX DAY 30): Erythrocytes: 4.76 [4.6 - 5.9] 10^12/L; Hematocrit: 0.333 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 99 [135 - 175] G/L; NPTST324-MEAN CELL HEMOGLOBIN: 20.8 [27 - 33] PG; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 29.7 [31 - 36] G/DL; NPTST329-MEAN CORPUSCULAR VOLUME: 70.0 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 10.0 [8.8 - 12.4] FL; NPTST431-RED CELL DISTRIBUTION WIDTH: 20.3 [11.5 - 14.5] %; NPTST528-WHOLE BLOOD GLUCOSE: 99 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 254 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 198 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 238 [70 - 100] MG/DL; Platelets: 433 [130 - 400] 10^9/L; [redacted]20[redacted](RX DAY 31): Erythrocytes: 4.01 [4.6 - 5.9] 10^12/L; Hematocrit: 0.278 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 83 [135 - 175] G/L; Leukocytes: 14.2 [4.8 - 10.8] 10^9/L; NPTST326-MEAN CORPUSCULAR HEMOGLOBIN: 20.7 [27 - 33] PG; NPTST327-MEAN CORPUSCULAR HEMOGLOBIN CON: 29.9 [31 - 36] G/DL; NPTST329-MEAN CORPUSCULAR VOLUME: 69.3 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 9.8 [8.8 - 12.4] FL; NPTST431-RED CELL DISTRIBUTION WIDTH: 19.5 [11.5 - 14.5] %; NPTST528-WHOLE BLOOD GLUCOSE: 172 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 251 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 199 [70 - 100] MG/DL; NPTST528-WHOLE BLOOD GLUCOSE: 160 [70 - 100] MG/DL; Platelets: 379 [130 - 400] 10^9/L; [redacted]20[redacted](RX DAY 32): Erythrocytes: 4.18 [4.6 - 5.9] 10^12/L; Hematocrit: 0.293 [0.41 - 0.51] FRACTION OF 1; Hemoglobin: 88 [135 - 175] G/L; Leukocytes: 14.23 [4.8 - 10.8] 10^9/L; Leukocytes: 29.8 [70 - 100] 10^9/L; NPTST325-MEAN CELL HEMOGLOBIN CONCENTRAT: 30.0 [31 - 36] G/DL; NPTST326-MEAN CORPUSCULAR HEMOGLOBIN: 21.1 [27 - 33] PG; NPTST329-MEAN CORPUSCULAR VOLUME: 70.1 [80 - 100] FL; NPTST331-MEAN PLATELET VOLUME: 10.2 [8.8 - 12.4] FL; NPTST431-RED CELL DISTRIBUTION WIDTH: 19.6 [11.5 - 14.5] %; NPTST528-WHOLE BLOOD GLUCOSE: 191 [70 - 100] MG/DL; Platelets: 419 [130 - 400] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 25): CT ABD PELVIS: DIFFUSE COLITIS UNCHANGED FROM PREVIOUS

AE Stopped Rx Day	32 (31 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DIFFUSE COLITIS FLARE FOLLOWING COLONOSCOPY SCREENING. POSSIBILITY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:10:36

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 3[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，投与初日＊　　，投与7日後＊　　，投与17日後＊及び 投与24日後＊　　にびまん性大腸炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，貧血，胃食道逆流性疾患，元喫煙者（1 日 1 箱を 5 年間）及び現飲酒者（1 日 2 杯未満）であった。

Event 1，2，3 及び 4 の臨床経過：

投与初日＊　，被験者はびまん性大腸炎を発現した。投与5日後＊　　，びまん性大腸炎は消失した。投与7日後＊　，被験者はびまん性大腸炎を発現した。投与12日後＊　　，びまん性大腸炎は消失した。投与17日後 ＊　　，被験者はびまん性大腸炎を発現した。投与20日後＊　　，びまん性大腸炎は消失した。投与24日後＊　，被験者はびまん性大腸炎を発現した。投与32日後＊，びまん性大腸炎は消失した。

投与1日後＊　，被験者は潰瘍性大腸炎に伴う慢性の間欠的腹痛があり，入院した。投与5日後＊ ，被験者は退院した。

投与7日後＊　，被験者は再入院した。被験者は 1 日に 7–8 回の血性の軟便をするようになり，疲労及び脱力が増大した。投与12日後＊，被験者の症状は安定し，退院した。

投与17日後＊　，被験者は腹痛の増大，血性の軟便及び右下腹部に限局した痛みのため，再入院した。被験者は CT スキャン検査，臨床検査及び身体検査を受けた。投与20日後＊　　，被験者は症状及び臨床検査値が正常化したため，退院した。

投与24日後＊　　，被験者は潰瘍性大腸炎の再燃があり，再入院した。被験者は脱力の増大，浮動性めまい，腹痛及び下痢を呈していた。被験者は CT スキャン検査，臨床検査及び身体検査を受けた。投与32日後＊，被験者は痛み及び臨床検査値が安定した後，退院した。

投与された薬剤は，コレカルシフェロール，lactobacillus acodoph/bulgaricus，酸化マグネシウム，硫酸鉄水和物，メチルプレドニゾロンコハク酸エステルナトリウム，アセトアミノフェン，ネオマイシン・ポリミキシン・バシトラシン合剤，prednisone，アザチオプリン，レボフラキサシン，塩化ナトリウム 0.9%，オキシコドン塩酸塩，バンコマイシン塩酸塩，ピペラシリン・タゾバクタム合剤及びヒドロモルフォンであった。

The patient's past medications include:

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

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

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

METOCLOPRAMIDE HCL for GERD ([redacted] 20[redacted]-[redacted] 20[redacted])

ONDANSETRON HCL for NAUSEA ([redacted] 20[redacted]-[redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Colitis (10009887) (Colitis (10009887)) [v.22.0] [10009887]

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

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

Dechallenge: Not Applicable

3) Colitis (10009887) (Colitis (10009887)) [v.22.0] [10009887]

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

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

Dechallenge: Not Applicable

4) Colitis (10009887) (Colitis (10009887)) [v.22.0] [10009887]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of DIFFUSE COLITIS

- Investigator: Combination of ulcerative colitis diagnosis and colonoscopy. May have induced a flare.

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

Event of DIFFUSE COLITIS

- Investigator: IT IS LIKELY THAT THE COLONOSCOPY INDUCED A FLARE.

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

Event of DIFFUSE COLITIS

- Investigator: PATIENT WAS EXPERIENCING A FLARE DUE TO UC DIAGNOSIS

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

Event of DIFFUSE COLITIS

- Investigator: DIFFUSE COLITIS FLARE FOLLOWING COLONOSCOPY SCREENING. POSSIBILITY

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted]ALBUMIN:** 2.9 G/DL (normal 3.5 to 5.0)

[redacted] **20[redacted]C REACTIVE PROTEIN HIGH SENS:** 24.196 mg/dL (normal 0 to 0.500)

[redacted] **20[redacted]C REACTIVE PROTEIN HIGH SENS:** 20.064 mg/dL (normal 0 to 0.500)

[redacted] **20[redacted]COLONOSCOPY:** Left sided UC

[redacted] **20[redacted]COLONOSCOPY:** Clear demarcation between normal and inflamed colonic mucosa seen

[redacted] **20[redacted]CREATININE:** 1.82 mg/dL (normal 0.72 to 1.25)

[redacted] **20[redacted]CREATININE:** 0.89 mg/dL (normal 0.72 to 1.25)

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** REDEMONSTRATION OF DIFFUSE COLITIS WITH SOME IMPROVEMENT FROM THE PRIOR STUDY

[redacted] **20[redacted]CT ABDOMEN AND PELVIS:** DIFFUSE COLITIS UNCHANGED FROM PREVIOUS

[redacted] **20[redacted]CT ABDOMINAL PELVIS:** Diffuse colitis

[redacted] **20[redacted]CT SCAN:** Showed diffuse colitis and backwash ileitis. Appendix was also inflamed.

[redacted] **20[redacted] CT SCAN:** CT SHOWS WALL THICKENING THROUGHOUT COLON WITH SURROUNDING INFLAMMATORY CHANGE CONSISTENT WITH INFECTIOUS VS INFLAMMATORY COLITIS, PHERINEPHRIC STRANDING AND STRANDING IN RETROPERITONEUM INCREASED COMPLARED TO PRIOR STUDY, APPENDIX IS DILATED WITH SURROUNDING INFLAMMATORY CHANGES SIMILAR TO PREVIOUS STUDY.

[redacted] **20[redacted]ESOPHAGOGASTRODUODENOSCOPY:** 2CM HIATAL HERNIA ESOPHAGITIS

[redacted] **20[redacted] GLUCOSE:** 139 mg/dL (normal 70 to 100)

[redacted] **20[redacted]GLUCOSE:** 157 mg/dL (normal 70 to 100)

[redacted] **20[redacted]GLUCOSE:** 127 mg/dL (normal 70 to 100)

[redacted] **20[redacted]GLUCOSE:** 320 mg/dL (normal 70 to 100)

[redacted] **20[redacted] HEMATOCRIT:** 34.9 % (normal 41 to 51)

[redacted] **20[redacted]HEMATOCRIT:** 28.7 % (normal 41 to 51)

[redacted] **20[redacted]HEMATOCRIT:** 31.2 % (normal 41 to 51)

[redacted] **20[redacted]HEMOGLOBIN:** 10.9 G/DL (normal 13.5 to 17.5)

[redacted] **20[redacted]HEMOGLOBIN:** 9.2 G/DL (normal 13.5 to 17.5)

[redacted] **20[redacted]HEMOGLOBIN:** 7.6 G/DL (normal 13.5 to 17.5)

[redacted] **20[redacted]INR:** 1.31 no units (normal 0.88 to 1.13)

[redacted] **20[redacted]LACTIC ACID:** 8.4 MMOL/L (normal 0.5 to 2.0)

[redacted] **20[redacted]LYMPHOCYTES** %: 15 % (normal 20 to 40)

[redacted] **20[redacted]LYMPHOCYTES** %: 10.60 % (normal 20 to 40)

[redacted] **20[redacted]MCV:** 67.5 FL (normal 80 to 100)

[redacted] **20[redacted] NEUTROPHILS ABS:** 10 X10**3/MCL (normal 2.4 to 8.1)

[redacted] **20[redacted]PLATELET COUNT:** 100 X10**3/MCL (normal 130 to 400)

[redacted] **20[redacted]PLATELET COUNT:** 116 X10**3/MCL (normal 130 to 400)

[redacted] **20[redacted]PLATELET COUNT:** 102 X10**3/MCL (normal 13.5 to 17.5)

[redacted] **20[redacted]PLATELET COUNT:** 348 X10**3/MCL (normal 13.5 to 17.5)

[redacted] 20[redacted] **POTASSIUM:** 3.0 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **POTASSIUM:** 3.4 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **PT:** 14.8 SEC (normal 9.7 to 12.3)

[redacted] 20[redacted] **RED BLOOD CELL DISTRIBUTION:** 15.6 % (normal 11.5 to 14.5)

[redacted] 20[redacted] **SODIUM:** 126 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] **SODIUM:** 126 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] **SODIUM:** 130 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] **URINE SPECIFIC GRAVITY:** 1.040 no units (normal 1.005 to 1.035)

[redacted] 20[redacted] **WBC:** 14.83 X10**3/MCL

[redacted] 20[redacted] **WBC:** 14.45 10^3/ul (normal 4.80 to 10.80)

[redacted] 20[redacted] **WBC:** 8.64 10^3/ul (normal 4.8 to 10.80)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 10.78 X10**3/MCL (normal 4.80 to 10.80)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 12.58 X10**3/MCL (normal 4.80 to 10.80)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 10.41 X10**3/MCL (normal 4.80 to 10.80)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 8.82 X10**3/MCL (normal 4.80 to 10.80)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 14.09 X10**3/MCL (normal 4.80 to 10.80)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 15.25 X10**3/MCL (normal 4.80 to 10.80)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 14.23 X10**3/MCL (normal 4.80 to 10.80)

M14-675 試験

治験の標題： 中等症から重症の活動性潰瘍性大腸炎患者を対象としたウパダシチニブ（ABT-494）の有効性及び安全性を評価する多施設共同無作為化二重盲検プラセボ対照導入療法試験
施設数 / 実施国名： 204 施設（アルゼンチン，オーストラリア，オーストリア，ベルギー，ボスニア・ヘルツェゴビナ，ブラジル，カナダ，チリ，中国，コロンビア，クロアチア，チェコ共和国，エストニア，フランス，ドイツ，ギリシャ，ハンガリー，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，ノルウェー，ポーランド，ポルトガル，ロシア，セルビア，シンガポール，スロバキア，南アフリカ，スペイン，スイス，台湾，トルコ，ウクライナ，イギリス及び米国［プエルトリコを含む］）
治験調整医師： [redacted], MD, PhD
公表文献（参考資料）： 11 報
治験期間： 最初の被験者の初回来院日：20[redacted] 年[redacted] 月[redacted] 日 最後の被験者の最終来院日：20[redacted] 年[redacted] 月[redacted] 日 開発のフェーズ： 第 III 相
目的： 中等症から重症の活動性潰瘍性大腸炎（以下「UC」）患者のうち，アミノサリチル酸製剤，免疫調節薬，副腎皮質ステロイド又は生物学的製剤に対して効果不十分，効果減弱又は不耐容であった患者を対象として，寛解導入（Adapted Mayo スコアによる）におけるウパダシチニブ 45 mg 1 日 1 回投与の有効性及び安全性をプラセボと比較して評価する。
被験者数（計画時と登録時）： 計画時：462 例，登録時：522 例
診断と主要な組入れ基準： 主要な選択基準：ベースライン時の年齢が 16 歳以上 75 歳以下の男女で，ベースラインの 90 日以上前に UC と診断され，スクリーニング期間中に全大腸内視鏡検査で診断が確認されると共に，現在の感染症，上皮異形成及び/又は悪性腫瘍が除外されている患者。Adapted Mayo スコアが 5–9，かつ内視鏡サブスコアが 2–3（中央判定による評価）の活動性 UC を有しており，経口アミノサリチル酸製剤，副腎皮質ステロイド，免疫調節薬及び/又は生物学的製剤のいずれかひとつ以上に対して効果不十分，効果減弱又は不耐容である患者。健康状態にその他の問題がない患者。 主要な除外基準：クローン病と診断されている患者。劇症の大腸炎及び/又は中毒性巨大結腸症と診断されている患者。病変が直腸のみに限局している患者。結腸全摘術若しくは結腸亜全摘術，回腸瘻，Kock パウチ又は回腸ストマ造設の既往がある患者，又は腸管の手術を予定している患者。副腎皮質ステロイド，免疫調節薬等の治験実施計画書に規定された併用禁止薬を投与された患者。
治験方法： 本試験は，中等症から重症の活動性 UC 患者を対象として，最長 16 週間の導入療法におけるウパダシチニブ 45 mg 経口投与の有効性及び安全性をプラセボと比較して評価する 2 つのパートで構成される第 III 相用量検証試験であった。8 週間の導入療法期である Part 1 では，被験者 522 例を 2：1 の比率で，二重盲検下でウパダシチニブ（345 例）又はプラセボ（177 例）のいずれかにランダム化した。ベースラインでの Bio-IR の状態（生物学的製剤に対して効果不十分，効果減弱又は不耐容［以下「Bio-IR」］，若しくは従来の治療に対して効果不十分，効果減弱又は不耐容を示すものの生物学的製剤は無効ではない［以下「Non-bio-IR」］），副腎皮質ステロイドの使用（あり又はなし）及び Adapted Mayo スコア（7 以下又は 7 超）を因子として層別化した。更に，Bio-IR については生物学的製剤の前治療歴（1 回以下又は 1 回超），Non-bio-IR については生物学的製剤の前治

療歴（あり又はなし）により層別化した。Part 1 の投与 8 週時に Adapted Mayo スコアによる臨床的改善を達成しなかった被験者は Part 2 に移行した。Part 2 では，すべての被験者（184 例）にウパダシチニブ 45 mg を投与した（Part 1 でプラセボ投与：116 例，Part 1 でウパダシチニブ 45 mg 投与：68 例）。

被験薬，用量，投与方法及びロット番号：

被験薬	用量	投与方法	バルクロット番号
ウパダシチニブ	45 mg	経口	[redacted], [redacted], [redacted]

治療期間：

Part 1：8 週間，Part 2：8 週間

対照薬，用量，投与方法及びロット番号：

ウパダシチニブに対応するプラセボの経口フィルムコート錠 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 8 週時の Adapted Mayo スコアによる臨床的寛解率（Adapted Mayo スコアが 2 以下で，排便回数サブスコア［以下「SFS」］が 1 以下かつベースラインを超えない，直腸出血サブスコア［以下「RBS」］が 0，かつ内視鏡サブスコアが 1 以下）とした。ただし，内視鏡検査中に脆弱性を示す所見が認められ，その他の内視鏡的活動が「軽度」の場合，内視鏡サブスコアは 2 とした。

順位付き副次評価項目は，投与 8 週時又は投与 2 週時（部分的 Adapted Mayo スコアによる臨床的改善率のみ）に評価した。

1. 内視鏡的改善率（内視鏡サブスコアが 0 又は 1）
2. 内視鏡的寛解率（内視鏡サブスコアが 0）
3. Adapted Mayo スコアによる臨床的改善率（Adapted Mayo スコアのベースラインからの減少が 2 以上かつ 30%以上，更に RBS の減少が 1 以上又は RBS が 1 以下）
4. 部分的 Adapted Mayo スコアによる臨床的改善率（部分的 Adapted Mayo スコアのベースラインからの減少が 1 以上かつ 30%以上，更に RBS の減少が 1 以上又は RBS が 1 以下）
5. 組織学的－内視鏡的粘膜改善率（内視鏡サブスコアが 1 以下及び Geboes スコアが 3.1 以下）
6. 便意切迫感を報告しなかった被験者の割合
7. 腹痛を報告しなかった被験者の割合
8. 組織学的改善率（Geboes スコアがベースラインから減少）
9. Inflammatory bowel disease questionnaire（以下「IBDQ」）合計スコアのベースラインからの変化量
10. 粘膜治癒率（内視鏡サブスコアが 0 及び Geboes スコアが 2 未満）
11. Functional assessment of chronic illness therapy-fatigue（以下「FACIT-F」）スコアのベースラインからの変化量

薬物動態：

ウパダシチニブ 45 mg 1 日 1 回投与後のウパダシチニブの血漿中濃度の平均値（標準偏差）を，前回投与からの時間ごとに要約した。

安全性：

有害事象，バイタルサイン，身体検査，臨床検査値（血液学的検査，血液生化学検査及び尿検査）及び治験薬に係る苦情を評価した。

統計手法：

有効性：

主要評価項目は，投与 8 週時の Adapted Mayo スコアによる臨床的寛解率とした。主要な estimand は，intent to

treat（以下「ITT」）集団を対象とした投与 8 週時の Adapted Mayo スコアによる臨床的寛解（治験薬の早期中止の有無は問わず，UC に関連する副腎皮質ステロイドの開始又は増量がない）を達成した被験者の割合に関するウパダシチニブ 45 mg 1 日 1 回群（以下「45 mg 群」）及びプラセボ 1 日 1 回群（以下「プラセボ群」）間の差とした。主要評価項目の解析では，欠測データを扱うための主要な解析手法としてノンレスポンダーインピュテーション（以下「NRI」）-C を用いた。NRI-C では，新型コロナウイルス感染症（以下「COVID-19」）又は COVID-19 感染拡大に関連する物流上の制限による欠測データは多重補完法を用い，それ以外の規定された来院の許容期間中に評価されなかった被験者（欠測又は試験の早期中止のいずれも）は非改善例として取り扱った。主要解析では，8 週間の二重盲検導入療法期である Part 1 でランダム化し，二重盲検下で治験薬を 1 回以上投与した被験者（以下「ITT1 集団」）を対象として 45 mg 群とプラセボ群間の臨床的寛解率を比較した。主要評価項目の投与群間差は，Bio-IR の状態（Bio-IR 又は Non-bio-IR），ベースラインでの副腎皮質ステロイドの使用（あり又はなし）及びベースラインでの Adapted Mayo スコア（7 以下又は 7 超）を層別因子とした Cochran Mantel Haenszel（以下「CMH」）検定を用いて評価した。臨床的寛解率の投与群間差について，CMH に基づいた両側 95%信頼区間を算出した。

主要評価項目の感度分析は，COVID-19 による欠測データを扱うための特別な解析手法を用いない NRI（NRI-NC），ハイブリッド多重補完法（HMI）及び as observed（以下「AO」）を用いて解析した。また，選択した逸脱が発生した被験者を除外した補足的な解析も実施した。

Part 1 の有効性の副次評価項目では ITT1 集団を対象とし，2 値変数の評価項目は CMH 検定により解析し，欠測データを扱うための主要な解析手法として NRI-C を用いた。感度分析は，NRI-NC を用いて解析した。連続変数の評価項目は，混合効果・反復測定モデル（MMRM）を用いて解析し，AO 及び Delta-Based Multiple Imputation（DBMI）（事後解析）を用いた解析も実施した。

薬物動態：

各来院時での被験者別のウパダシチニブの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。

安全性：

標準的な安全性解析として，有害事象，特に注目すべき有害事象，臨床検査値及びバイタルサインを評価した。安全性解析対象集団（Part 1 の被験者［SA1 集団］，Part 2 の被験者［SA2 集団］）を対象として，安全性についてウパダシチニブ群とプラセボ群間の比較を行った。安全性評価項目は，実際の投与に基づいた投与群ごとに要約した。有害事象については，投与群別に ICH 国際医薬用語集（MedDRA）version 23.0 を用いて発現被験者数及び発現割合を要約した。安全性評価項目の連続変数（臨床検査値及びバイタルサインのベースラインからの変化量等）の投与群間差は，投与群を項とする分散分析モデルを用いて評価した。

有効性の結果

投与 8 週時に評価するすべての評価項目及び投与 2 週時の部分的 Adapted Mayo スコアによる臨床的改善率について，プラセボ群と比較して 45 mg 群で統計学的に有意な改善が認められ（$P < 0.001$），主要評価項目である Adapted Mayo スコアによる臨床的寛解率及びすべての順位付き副次評価項目を達成した。これらの評価項目から，疾患活動性及び症状，内視鏡的及び組織学的評価，炎症のバイオマーカー並びに生活の質（以下「QOL」）などの様々な領域の改善について，プラセボ群と比較して 45 mg 群で高い有効性が示された。また，Part 1 でウパダシチニブ 45 mg を 8 週間投与し，臨床的改善を達成しなかった被験者では，Part 2 の投与 16 週時の Adapted Mayo スコアによる臨床的改善率は 45.5%（30/66 例）であった。これより，ウパダシチニブ 45 mg 1 日 1 回投与による導入療法の投与 8 週時までに臨床的改善を達成しなかった被験者でも，投与 16 週時まで延長投与することにより，ベネフィットが得られる可能性が示された。

ウパダシチニブ 45 mg 1 日 1 回投与による 8 週間の導入療法を受けた被験者では，IBDQ，European Quality of Life-5 Dimensions 5 Levels（EQ-5D-5L），Work Productivity and Activity Impairment Questionnaire（WPAI），FACIT-F，Ulcerative Colitis Symptoms Questionnaire（UC-SQ）及び 36-item short-form health survey（SF-36）のベースラインからの変化量はプラセボ群と比較して 45 mg 群の方が大きく，QOL に関するすべての評価項目でもベースラインからの大きな改善が認められた。これらの改善は投与 2 週時と早期から認められた。

以上の結果から，ウパダシチニブ 45 mg 1 日 1 回投与は，中等症から重症の活動性 UC 患者を対象とした導入療法として有効であることが示された。

薬物動態の結果

ウパダシチニブの血漿中濃度の平均値は，ウパダシチニブ 45 mg 1 日 1 回投与後 24 時間以内で 12.2–98.5 ng/mL の範囲であった。ウパダシチニブの血漿中濃度は，過去にウパダシチニブの試験で認められた薬物動態と一致していた。

安全性の結果

- Part 1 では，有害事象及び治験薬と関連ありの有害事象の発現割合は，プラセボ群と比較して 45 mg 群の方が高かった。重篤な有害事象，高度の有害事象及び治験薬の投与中止に至った有害事象の発現割合は，プラセボ群と比較して 45 mg 群の方が低かった。死亡は認められなかった。特に注目すべき有害事象の日和見感染（結核及び帯状疱疹を除く），帯状疱疹，好中球減少症，クレアチンホスホキナーゼ増加，薬剤に関連する肝障害，貧血及びリンパ球減少症の発現割合は，プラセボ群と比較して 45 mg 群の方が高かった。
- Part 1 では，発現割合が 5%以上であった有害事象は，プラセボ群では頭痛であった。Part 1 で 45 mg 群で多く認められた（発現割合が 4%以上）有害事象は，ざ瘡，血中クレアチンホスホキナーゼ増加及び貧血であった。
- Part 1 では，重篤な有害事象の発現割合はプラセボ群で 4.5%であり，45 mg 群で 4%未満であった。最も多く認められた重篤な有害事象は，潰瘍性大腸炎であった。
- Part 1 及び Part 2 では，特に注目すべき有害事象のうち，活動性結核，悪性腫瘍，非黒色腫皮膚癌（以下「NMSC」）を除く悪性腫瘍，NMSC，リンパ腫，腎機能障害，主要心血管事象は認められなかった。Part 1 では，クレアチンホスホキナーゼ増加の発現割合は，プラセボ群（1.1%，2 例）と比較して 45 mg 群（4.7%，16 例）の方が高かった。好中球減少症，リンパ球減少症，貧血及び薬剤に関連する肝障害の発現割合も，プラセボ群（それぞれ 0%，0.6%，2.3%及び 0.6%）と比較して 45 mg 群（それぞれ 4.4%，1.7%，4.4%及び 2.9%）の方が高かったが，消化管穿孔及び静脈血栓塞栓症の発現割合は，プラセボ群（いずれも 0.6%）と比較して 45 mg 群（いずれも 0%）の方が低かった。
- Part 1 では，投与 8 週時の血液学的検査のベースラインからの平均変化量（最小二乗平均）について，ヘモグロビン量，血小板数及び好中球数は，プラセボ群と比較し

て 45 mg 群で大きな減少が認められた。リンパ球数は，45 mg 群とプラセボ群で同程度の減少が認められた。

- Part 1 では，投与 8 週時の血液生化学検査のベースラインからの平均変化量について，アスパラギン酸アミノトランスフェラーゼ（AST），アラニンアミノトランスフェラーゼ（ALT），クレアチンキナーゼ，クレアチニン及びコレステロールは，プラセボ群と比較して 45 mg 群で増加が認められた。
- Part 1 では，Grade 3 のヘモグロビン量減少が認められた被験者の割合は，45 mg 群と比較してプラセボ群の方が高かった。Grade 3 の好中球数減少又はリンパ球数減少が認められた被験者の割合は，プラセボ群と比較して 45 mg 群の方が高かった。Grade 3 の血小板数減少又は白血球数減少，及び Grade 4 のヘモグロビン量，血小板数，白血球数，好中球数又はリンパ球数減少が認められた被験者はいなかった。
- Part 1 では，45 mg 群で最も多く認められた臨床的な意義があると判断したバイタルサインは，7%超の体重増加であり，その割合はプラセボ群（2.3%）と比較して 45 mg 群（9.3%）で高かった。
- Part 2 では，投与 16 週時までのウパダシチニブ 45 mg 1 日 1 回投与は，全体として安全性リスクを増加させなかった。

結論

導入療法としてのウパダシチニブ 45 mg 1 日 1 回，8 週間の投与は，主要評価項目の臨床的寛解率及びすべての順位付き副次評価項目で，プラセボと比較して統計学的に有意に高い改善効果を示した。また，疾患活動性及び症状，内視鏡的及び組織学的評価，炎症のバイオマーカー並びに QOL に関する評価項目でも，ウパダシチニブの有効性が示された。

導入療法としてのウパダシチニブ 45 mg 1 日 1 回投与は，おおむね安全で忍容性は良好であった。ウパダシチニブの既知の安全性プロファイルと比較して，新たな安全性のリスクは認められなかった。

本試験では 18 歳未満の被験者を 9 例登録し，6 例を 45 mg 群，3 例をプラセボ群にランダム化した。18 歳未満の被験者数は少なかったため，有効性及び安全性を結論付けることはできなかった。これらの被験者で報告された有害事象は，プラセボ群で 4 件，45 mg 群で 3 件であった。このうち，プラセボ群の 1 件（貧血）は重篤な有害事象であった。新たな安全性シグナルは特定されなかった。

本試験の結果は，中等症から重症の活動性 UC 患者を対象とした導入療法として，ウパダシチニブ 45 mg 1 日 1 回投与を裏付けるものであった。

日本人部分集団の有害事象

日本人部分集団の有害事象の発現状況を以下に示す。

Part 1

有害事象の発現割合は，45 mg 群で 61.5%（32/52 例），プラセボ群で 37.9%（11/29 例）であった。多く認められた（発現割合が 5%以上）有害事象は，45 mg 群でざ瘡，口内炎，発熱，好中球減少症，血中クレアチンホスホキナーゼ増加，好中球数減少，上咽頭炎及び毛包炎であり，プラセボ群で上咽頭炎及び潰瘍性大腸炎であった。

治験薬と関連ありの有害事象は，45 mg 群で 32.7%（17 例）に認められ，プラセボ群では認められなかった。45 mg 群で多く認められた（発現割合が 5%以上）治験薬と関連ありの有害事象は，好中球減少症，好中球数減少及びざ瘡であった。

高度の有害事象の発現割合は，45 mg 群で 3.8%（2 例），プラセボ群で 3.4%（1 例）であった。45 mg 群で 2 例以上に認められた高度の有害事象はなかった。

死亡に至った有害事象は認められなかった。

重篤な有害事象の発現割合は，45 mg 群で 3.8%（2 例），プラセボ群で 6.9%（2 例）であった。いずれの投与群でも，2 例以上に認められた重篤な有害事象はなかった。

治験薬の投与中止に至った有害事象の発現割合は，45 mg 群で 1.9%（1 例），プラセボ群で 3.4%（1 例）であった。

Part 2

有害事象の発現割合は，Part 1 及び Part 2 でウパダシチニブ 45 mg を 1 日 1 回投与した群（以下「45 mg/45 mg 群」）で 57.1%（4/7 例），Part 1 でプラセボ，Part 2 でウパダシチニブ 45 mg を 1 日 1 回投与した群（以下「プラセボ/45 mg 群」）で 45.0%（9/20 例）であった。2 例以上に認められた有害事象は，45 mg/45 mg 群で血中クレアチンホスホキナーゼ増加であり，プラセボ/45 mg 群でインフルエンザ及びざ瘡であった。

治験薬と関連ありの有害事象の発現割合は，45 mg/45 mg 群で 28.6%（2 例），プラセボ/45 mg 群で 10.0%（2 例）であった。いずれの投与群でも，2 例以上に認められた治験薬と関連ありの有害事象はなかった。

高度の有害事象は認められなかった。

死亡に至った有害事象は認められなかった。

重篤な有害事象は認められなかった。

治験薬の投与中止に至った有害事象は認められなかった。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団	日本人部分集団
有害事象の概要	表 1 (TABLE 14.3__1.1.1)	表 8 (TABLE 14.3__1.1.1_J)
すべての有害事象	表 2 (TABLE 14.3__1.2.1.1)	表 9 (TABLE 14.3__1.2.1.1_J)
治験薬と関連ありの有害事象	表 3 (TABLE 14.3__1.3.1.1)	表 10 (TABLE 14.3__1.3.1.1_J)
高度の有害事象	表 4 (TABLE 14.3__1.3.3)	表 11 (TABLE 14.3__1.3.3_J)
死亡に至った有害事象	表 5 (TABLE 14.3__2.3.1)	表 12 (TABLE 14.3__2.3.1_J)
重篤な有害事象	表 6 (TABLE 14.3__2.1.1)	表 13 (TABLE 14.3__2.1.1_J)
治験薬の投与中止に至った有害事象	表 7 (TABLE 14.3__2.2.1)	表 14 (TABLE 14.3__2.2.1_J)

表1

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.1

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1 Population and SA2 Population)

	Part 1			Part 2	
	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Difference UPA - Placebo (95% CI&)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
Subjects with:					
Any adverse event (AE)	70 (39.5)	182 (52.9)	13.4 (4.4, 22.3)	52 (44.8)	28 (41.2)
Any AE with reasonable possibility of being related to study drug$	12 (6.8)	81 (23.5)	16.8 (11.0, 22.6)	17 (14.7)	11 (16.2)
Any severe AE	7 (4.0)	9 (2.6)	-1.3 (-4.7, 2.0)	2 (1.7)	0
Any serious AE	8 (4.5)	11 (3.2)	-1.3 (-4.9, 2.3)	4 (3.4)	1 (1.5)
Any AE leading to discontinuation of study drug	9 (5.1)	6 (1.7)	-3.3 (-6.9, 0.2)	2 (1.7)	2 (2.9)
Any AE leading to death	0	0	0.0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
& 95% CI for treatment difference is based on the normal approximation.

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TABLE 14.3 1.1.1

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1 Population and SA2 Population)

	Part 1			Part 2	
	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Difference UPA - Placebo (95% CI&)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
Subjects with:					
Deaths#	0	0	0.0	0	0
Occurring <= 30 days after last dose	0	0	0.0	0	0
Occurring > 30 days after last dose	0	0	0.0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
& 95% CI for treatment difference is based on the normal approximation.

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表2

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3__1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
Any adverse event	70 (39.5)	182 (52.9)	52 (44.8)	28 (41.2)
血液およびリンパ系障害	5 (2.8)	27 (7.8)	7 (6.0)	6 (8.8)
貧血	4 (2.3)	14 (4.1)	3 (2.6)	4 (5.9)
内出血発生の増加傾向	0	1 (0.3)	0	0
鉄欠乏性貧血	0	0	1 (0.9)	0
白血球減少症	1 (0.6)	1 (0.3)	2 (1.7)	0
リンパ節痛	0	1 (0.3)	0	0
リンパ球減少症	1 (0.6)	4 (1.2)	1 (0.9)	1 (1.5)
好中球減少症	0	6 (1.7)	1 (0.9)	0
血小板減少症	0	1 (0.3)	0	1 (1.5)
血小板増加症	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

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TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
心臓障害	2 (1.1)	2 (0.6)	1 (0.9)	0
動悸	1 (0.6)	2 (0.6)	0	0
洞性不整脈	1 (0.6)	0	0	0
洞性頻脈	0	0	1 (0.9)	0
頻脈	1 (0.6)	0	0	0
耳および迷路障害	1 (0.6)	2 (0.6)	0	0
耳痛	1 (0.6)	0	0	0
聴力低下	0	1 (0.3)	0	0
突発性難聴	0	1 (0.3)	0	0
耳鳴	0	2 (0.6)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

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TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
眼障害	4 (2.3)	7 (2.0)	1 (0.9)	0
眼瞼炎	0	1 (0.3)	0	0
結膜出血	0	1 (0.3)	0	0
ドライアイ	0	1 (0.3)	1 (0.9)	0
眼のアレルギー	1 (0.6)	0	0	0
角膜炎	0	1 (0.3)	0	0
流涙増加	1 (0.6)	0	0	0
眼部不快感	1 (0.6)	0	0	0
眼充血	0	1 (0.3)	0	0
翼状片	1 (0.6)	0	0	0
霧視	1 (0.6)	2 (0.6)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

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TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
胃腸障害	26 (14.7)	46 (13.4)	11 (9.5)	5 (7.4)
腹部不快感	0	0	1 (0.9)	0
腹部膨満	1 (0.6)	2 (0.6)	1 (0.9)	0
腹痛	1 (0.6)	5 (1.5)	1 (0.9)	1 (1.5)
下腹部痛	0	1 (0.3)	1 (0.9)	0
上腹部痛	2 (1.1)	1 (0.3)	0	0
裂肛	1 (0.6)	2 (0.6)	1 (0.9)	0
アフタ性潰瘍	2 (1.1)	2 (0.6)	0	0
大腸炎	1 (0.6)	0	0	0
潰瘍性大腸炎	8 (4.5)	6 (1.7)	2 (1.7)	3 (4.4)
便秘	2 (1.1)	5 (1.5)	1 (0.9)	0
齲歯	1 (0.6)	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

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TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
胃腸障害 (Cont.)				
下痢	0	3 (0.9)	1 (0.9)	0
血性下痢	0	1 (0.3)	0	0
口内乾燥	0	2 (0.6)	0	0
消化不良	1 (0.6)	1 (0.3)	0	0
鼓腸	1 (0.6)	1 (0.3)	1 (0.9)	0
食中毒	0	1 (0.3)	0	0
びらん性胃炎	0	1 (0.3)	0	0
胃食道逆流性疾患	1 (0.6)	3 (0.9)	0	1 (1.5)
歯肉痛	0	0	0	1 (1.5)
歯肉腫脹	0	1 (0.3)	0	0
痔出血	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

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TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
胃腸障害 (Cont.)				
痔核	2 (1.1)	5 (1.5)	0	0
胃酸過多	0	1 (0.3)	0	0
大腸穿孔	1 (0.6)	0	0	0
大腸ポリープ	0	0	0	1 (1.5)
口腔内潰瘍形成	0	0	1 (0.9)	0
悪心	4 (2.3)	3 (0.9)	1 (0.9)	0
口腔内痛	0	1 (0.3)	0	1 (1.5)
歯周病	0	1 (0.3)	0	0
肛門周囲痛	0	1 (0.3)	0	0
偽性ポリポーシス	0	1 (0.3)	0	0
口内炎	1 (0.6)	4 (1.2)	3 (2.6)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
胃腸障害 (Cont.)				
歯痛	0	1 (0.3)	0	0
嘔吐	1 (0.6)	0	2 (1.7)	0
一般・全身障害および投与部位の状態	8 (4.5)	19 (5.5)	4 (3.4)	4 (5.9)
無力症	1 (0.6)	2 (0.6)	0	0
胸部不快感	0	0	0	1 (1.5)
胸痛	0	1 (0.3)	0	0
悪寒	1 (0.6)	0	0	0
疲労	3 (1.7)	6 (1.7)	0	0
インフルエンザ様疾患	0	1 (0.3)	0	0
注入部位反応	0	1 (0.3)	0	0
末梢性浮腫	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
疼痛	1 (0.6)	0	0	0
末梢腫脹	0	1 (0.3)	0	0
偽ポリープ	0	1 (0.3)	0	0
発熱	3 (1.7)	8 (2.3)	4 (3.4)	4 (5.9)
顔面腫脹	1 (0.6)	1 (0.3)	0	0
ワクチン接種部位紅斑	1 (0.6)	0	0	0
ワクチン接種部位疼痛	1 (0.6)	0	0	0
肝胆道系障害	1 (0.6)	1 (0.3)	0	0
肝機能異常	0	1 (0.3)	0	0
高ビリルビン血症	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
免疫系障害	0	1 (0.3)	0	0
季節性アレルギー	0	1 (0.3)	0	0
感染症および寄生虫症	16 (9.0)	58 (16.9)	22 (19.0)	11 (16.2)
細菌性膣症	1 (0.6)	0	0	0
体部白癬	0	1 (0.3)	0	0
ボレリア感染	0	1 (0.3)	0	0
気管支炎	0	1 (0.3)	0	0
クロストリジウム・ディフィシレ感染	0	0	0	1 (1.5)
ウイルス性結膜炎	1 (0.6)	0	0	0
COVID－19	0	0	0	1 (1.5)
COVID－19肺炎	0	1 (0.3)	1 (0.9)	0
サイトメガロウイルス性大腸炎	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
感染症および寄生虫症 (Cont.)				
サイトメガロウイルス感染	0	1 (0.3)	0	0
毛嚢虫症	0	0	1 (0.9)	0
デング熱	0	1 (0.3)	0	0
耳感染	0	1 (0.3)	0	0
腸球菌感染	1 (0.6)	0	0	0
大腸菌感染	1 (0.6)	0	0	0
毛包炎	0	7 (2.0)	2 (1.7)	0
せつ	0	1 (0.3)	0	0
胃腸炎	0	0	0	2 (2.9)
ウイルス性胃腸炎	0	0	1 (0.9)	1 (1.5)
陰部ヘルペス	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
感染症および寄生虫症 (Cont.)				
単純ヘルペス	0	2 (0.6)	1 (0.9)	0
帯状疱疹	0	2 (0.6)	0	1 (1.5)
麦粒腫	1 (0.6)	0	1 (0.9)	0
膿痂疹	0	0	0	1 (1.5)
インフルエンザ	0	3 (0.9)	3 (2.6)	1 (1.5)
上咽頭炎	4 (2.3)	13 (3.8)	2 (1.7)	1 (1.5)
口腔カンジダ症	0	0	1 (0.9)	0
口腔ヘルペス	0	4 (1.2)	2 (1.7)	1 (1.5)
急性中耳炎	0	0	1 (0.9)	0
歯周炎	0	0	1 (0.9)	0
咽頭炎	0	0	0	1 (1.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
感染症および寄生虫症 (Cont.)				
レンサ球菌性咽頭炎	0	0	1 (0.9)	0
毛巣嚢胞	0	0	1 (0.9)	0
肺炎	0	1 (0.3)	0	0
処置後感染	1 (0.6)	0	0	0
歯髄炎	1 (0.6)	0	0	0
膿疱	0	1 (0.3)	0	0
腎盂腎炎	0	1 (0.3)	0	0
膿尿	1 (0.6)	0	0	0
膿疱性皮疹	0	0	1 (0.9)	0
気道感染	0	1 (0.3)	0	0
ウイルス性気道感染	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
感染症および寄生虫症 (Cont.)				
副鼻腔炎	1 (0.6)	1 (0.3)	0	0
股部白癬	0	0	1 (0.9)	0
白癬感染	0	0	0	1 (1.5)
扁桃炎	0	0	1 (0.9)	0
歯膿瘍	0	1 (0.3)	0	0
歯感染	0	1 (0.3)	0	0
上気道感染	1 (0.6)	7 (2.0)	2 (1.7)	2 (2.9)
尿路感染	4 (2.3)	4 (1.2)	0	0
ウイルス感染	0	0	1 (0.9)	0
外陰部腟カンジダ症	0	1 (0.3)	0	1 (1.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
傷害、中毒および処置合併症	3 (1.7)	6 (1.7)	1 (0.9)	2 (2.9)
挫傷	1 (0.6)	1 (0.3)	0	1 (1.5)
転倒	0	0	1 (0.9)	0
消化管ストーマ壊死	1 (0.6)	0	0	0
手骨折	0	1 (0.3)	0	0
損傷	0	0	0	1 (1.5)
靱帯捻挫	1 (0.6)	2 (0.6)	0	1 (1.5)
肋骨骨折	0	0	0	1 (1.5)
皮膚擦過傷	0	1 (0.3)	0	0
皮膚裂傷	0	0	1 (0.9)	0
脊柱損傷	0	0	1 (0.9)	0
創傷	0	2 (0.6)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
臨床検査	4 (2.3)	41 (11.9)	10 (8.6)	9 (13.2)
アラニンアミノトランスフェラーゼ増加	0	3 (0.9)	2 (1.7)	0
アミラーゼ増加	0	1 (0.3)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	5 (1.5)	1 (0.9)	0
血中アルカリホスファターゼ増加	0	1 (0.3)	0	0
血中ビリルビン増加	0	1 (0.3)	0	0
血中クロール減少	0	1 (0.3)	0	0
血中コレステロール増加	0	1 (0.3)	0	0
血中クレアチンホスホキナーゼ増加	2 (1.1)	16 (4.7)	5 (4.3)	4 (5.9)
血中クレアチニン増加	1 (0.6)	2 (0.6)	0	0
血中ブドウ糖増加	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
臨床検査 (Cont.)				
血中リン減少	0	3 (0.9)	0	0
血中尿酸増加	0	0	1 (0.9)	0
体温上昇	0	1 (0.3)	0	0
クロストリジウム検査陽性	0	1 (0.3)	1 (0.9)	1 (1.5)
γ－グルタミルトランスフェラーゼ増加	1 (0.6)	2 (0.6)	0	0
糸球体濾過率減少	0	1 (0.3)	0	1 (1.5)
ヘモグロビン減少	0	1 (0.3)	0	0
肝酵素上昇	0	1 (0.3)	0	2 (2.9)
眼圧上昇	0	1 (0.3)	0	0
リンパ球数減少	0	2 (0.6)	0	0
リンパ球数増加	0	0	1 (0.9)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
臨床検査 (Cont.)				
リンパ球百分率減少	0	1 (0.3)	0	0
好中球数減少	0	9 (2.6)	0	1 (1.5)
血小板数減少	0	1 (0.3)	0	0
トランスアミナーゼ上昇	0	1 (0.3)	0	0
ビタミンD減少	0	0	1 (0.9)	0
体重増加	0	1 (0.3)	0	1 (1.5)
白血球数減少	0	7 (2.0)	0	1 (1.5)
白血球数増加	0	1 (0.3)	0	0
代謝および栄養障害	4 (2.3)	6 (1.7)	1 (0.9)	1 (1.5)
食欲減退	0	1 (0.3)	0	0
糖尿病	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
代謝および栄養障害 (Cont.)				
痛風	0	1 (0.3)	0	0
高コレステロール血症	1 (0.6)	0	0	0
高血糖	1 (0.6)	0	0	0
高カリウム血症	0	1 (0.3)	0	0
高尿酸血症	1 (0.6)	1 (0.3)	0	0
低ナトリウム血症	0	1 (0.3)	0	0
低リン酸血症	0	0	1 (0.9)	0
低蛋白血症	0	0	0	1 (1.5)
栄養障害	0	1 (0.3)	0	0
筋骨格系および結合組織障害	18 (10.2)	18 (5.2)	3 (2.6)	3 (4.4)
関節痛	3 (1.7)	5 (1.5)	3 (2.6)	2 (2.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
筋骨格系および結合組織障害 (Cont.)				
関節炎	0	2 (0.6)	0	0
関節障害	5 (2.8)	1 (0.3)	0	0
背部痛	1 (0.6)	2 (0.6)	0	1 (1.5)
滑液包炎	1 (0.6)	0	0	0
尾骨痛	0	1 (0.3)	0	0
側腹部痛	0	1 (0.3)	0	0
関節弛緩	0	0	1 (0.9)	0
関節ロック	0	0	1 (0.9)	0
関節腫脹	1 (0.6)	0	0	0
筋拘縮	0	1 (0.3)	0	0
筋障害	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
筋骨格系および結合組織障害 (Cont.)				
筋痙縮	3 (1.7)	1 (0.3)	0	0
筋骨格系胸痛	0	1 (0.3)	0	0
筋骨格不快感	0	1 (0.3)	0	0
筋肉痛	1 (0.6)	1 (0.3)	1 (0.9)	0
頚部痛	1 (0.6)	0	0	0
変形性関節症	1 (0.6)	0	0	0
四肢痛	2 (1.1)	0	0	0
病的骨折	0	1 (0.3)	0	0
脊椎関節障害	1 (0.6)	0	0	0
弾発指	0	1 (0.3)	0	0
開口障害	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	1 (0.9)	0
脂肪腫	0	0	1 (0.9)	0
神経系障害	11 (6.2)	16 (4.7)	5 (4.3)	2 (2.9)
灼熱感	0	1 (0.3)	0	0
脳虚血	0	1 (0.3)	0	0
浮動性めまい	0	2 (0.6)	0	1 (1.5)
頭痛	9 (5.1)	8 (2.3)	2 (1.7)	2 (2.9)
感覚鈍麻	0	2 (0.6)	0	0
片頭痛	1 (0.6)	1 (0.3)	1 (0.9)	0
末梢性ニューロパチー	0	1 (0.3)	0	0
錯感覚	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
神経系障害 (Cont.)				
失神寸前の状態	1 (0.6)	0	0	0
傾眠	0	1 (0.3)	0	0
失神	0	0	1 (0.9)	0
味覚障害	0	1 (0.3)	0	0
振戦	0	0	1 (0.9)	0
精神障害	7 (4.0)	7 (2.0)	1 (0.9)	1 (1.5)
急性精神病	0	1 (0.3)	0	0
不安	4 (2.3)	1 (0.3)	1 (0.9)	0
不安障害	0	0	0	1 (1.5)
うつ病	1 (0.6)	1 (0.3)	1 (0.9)	0
不眠症	2 (1.1)	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
精神障害 (Cont.)				
リビドー減退	0	1 (0.3)	0	0
悪夢	0	1 (0.3)	0	0
パニック発作	1 (0.6)	0	0	0
睡眠障害	1 (0.6)	1 (0.3)	0	0
腎および尿路障害	0	2 (0.6)	0	0
排尿困難	0	1 (0.3)	0	0
尿管結石症	0	1 (0.3)	0	0
生殖系および乳房障害	0	5 (1.5)	1 (0.9)	0
無月経	0	1 (0.3)	0	0
良性前立腺肥大症	0	1 (0.3)	0	0
不規則月経	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
生殖系および乳房障害 (Cont.)				
月経前頭痛	0	0	1 (0.9)	0
精液変色	0	1 (0.3)	0	0
精索静脈瘤	0	1 (0.3)	0	0
呼吸器、胸郭および縦隔障害	9 (5.1)	5 (1.5)	2 (1.7)	3 (4.4)
慢性閉塞性肺疾患	1 (0.6)	0	1 (0.9)	0
咳嗽	2 (1.1)	2 (0.6)	1 (0.9)	1 (1.5)
横隔膜痛	1 (0.6)	0	0	0
呼吸困難	0	1 (0.3)	0	0
鼻閉	1 (0.6)	0	0	0
口腔咽頭痛	1 (0.6)	1 (0.3)	0	0
副鼻腔不快感	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
湿性咳嗽	0	0	0	1 (1.5)
肺塞栓症	1 (0.6)	0	0	0
鼻痛	0	0	0	1 (1.5)
アレルギー性鼻炎	0	1 (0.3)	0	0
副鼻腔うっ血	3 (1.7)	0	0	0
上気道咳症候群	1 (0.6)	0	0	0
皮膚および皮下組織障害	11 (6.2)	46 (13.4)	11 (9.5)	5 (7.4)
ざ瘡	3 (1.7)	24 (7.0)	6 (5.2)	0
脱毛症	0	2 (0.6)	0	1 (1.5)
アンドロゲン性脱毛症	0	1 (0.3)	0	0
皮膚炎	1 (0.6)	0	0	1 (1.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
皮膚および皮下組織障害 (Cont.)				
ざ瘡様皮膚炎	0	1 (0.3)	0	0
皮膚乾燥	1 (0.6)	0	0	0
湿疹	2 (1.1)	1 (0.3)	0	0
固定疹	0	0	0	1 (1.5)
多汗症	1 (0.6)	0	0	0
汗疹	0	1 (0.3)	0	0
寝汗	1 (0.6)	0	0	0
丘疹	0	0	0	1 (1.5)
光線過敏性反応	0	1 (0.3)	0	0
そう痒症	1 (0.6)	2 (0.6)	0	0
壊疽性膿皮症	1 (0.6)	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
皮膚および皮下組織障害 (Cont.)				
発疹	1 (0.6)	8 (2.3)	4 (3.4)	0
紅斑性皮疹	1 (0.6)	0	0	0
斑状丘疹状皮疹	0	1 (0.3)	0	0
丘疹性皮疹	0	2 (0.6)	0	0
酒さ	0	0	0	1 (1.5)
脂漏性皮膚炎	0	3 (0.9)	1 (0.9)	0
皮膚病変	0	1 (0.3)	0	0
皮膚潰瘍	0	0	1 (0.9)	0
毛細血管拡張症	0	0	0	1 (1.5)
尋常性白斑	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
血管障害	4 (2.3)	2 (0.6)	1 (0.9)	2 (2.9)
本態性高血圧症	0	0	0	1 (1.5)
潮紅	1 (0.6)	0	0	1 (1.5)
血腫	1 (0.6)	0	0	0
ほてり	0	1 (0.3)	0	0
高血圧	1 (0.6)	2 (0.6)	0	0
骨盤静脈血栓症	1 (0.6)	0	0	0
血栓性静脈炎	0	0	1 (0.9)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表3

TABLE 14.3__1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
Any adverse event	12 (6.8)	81 (23.5)	17 (14.7)	11 (16.2)
血液およびリンパ系障害	2 (1.1)	11 (3.2)	1 (0.9)	1 (1.5)
貧血	2 (1.1)	2 (0.6)	0	0
白血球減少症	0	1 (0.3)	1 (0.9)	0
リンパ節痛	0	1 (0.3)	0	0
リンパ球減少症	0	2 (0.6)	0	1 (1.5)
好中球減少症	0	6 (1.7)	0	0
耳および迷路障害	1 (0.6)	2 (0.6)	0	0
耳痛	1 (0.6)	0	0	0
聴力低下	0	1 (0.3)	0	0
突発性難聴	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
耳および迷路障害 (Cont.)				
耳鳴	0	2 (0.6)	0	0
眼障害	1 (0.6)	4 (1.2)	1 (0.9)	0
眼瞼炎	0	1 (0.3)	0	0
ドライアイ	0	0	1 (0.9)	0
角膜炎	0	1 (0.3)	0	0
眼部不快感	1 (0.6)	0	0	0
霧視	0	2 (0.6)	0	0
胃腸障害	3 (1.7)	11 (3.2)	2 (1.7)	2 (2.9)
腹痛	0	2 (0.6)	0	1 (1.5)
下腹部痛	0	1 (0.3)	0	0
上腹部痛	1 (0.6)	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
胃腸障害 (Cont.)				
アフタ性潰瘍	0	2 (0.6)	0	0
潰瘍性大腸炎	0	1 (0.3)	1 (0.9)	2 (2.9)
便秘	0	1 (0.3)	0	0
下痢	0	2 (0.6)	0	0
血性下痢	0	1 (0.3)	0	0
消化不良	1 (0.6)	0	0	0
鼓腸	0	0	1 (0.9)	0
胃食道逆流性疾患	0	1 (0.3)	0	0
痔核	0	1 (0.3)	0	0
悪心	1 (0.6)	2 (0.6)	0	0
口内炎	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
一般・全身障害および投与部位の状態	1 (0.6)	5 (1.5)	1 (0.9)	0
無力症	1 (0.6)	2 (0.6)	0	0
疲労	1 (0.6)	3 (0.9)	0	0
発熱	0	1 (0.3)	1 (0.9)	0
感染症および寄生虫症	1 (0.6)	15 (4.4)	7 (6.0)	2 (2.9)
毛嚢虫症	0	0	1 (0.9)	0
毛包炎	0	1 (0.3)	2 (1.7)	0
単純ヘルペス	0	1 (0.3)	1 (0.9)	0
帯状疱疹	0	1 (0.3)	0	1 (1.5)
インフルエンザ	0	0	1 (0.9)	0
上咽頭炎	1 (0.6)	2 (0.6)	1 (0.9)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
感染症および寄生虫症 (Cont.)				
口腔ヘルペス	0	2 (0.6)	0	0
急性中耳炎	0	0	1 (0.9)	0
肺炎	0	1 (0.3)	0	0
膿疱	0	1 (0.3)	0	0
気道感染	0	1 (0.3)	0	0
副鼻腔炎	0	1 (0.3)	0	0
上気道感染	0	3 (0.9)	0	1 (1.5)
ウイルス感染	0	0	1 (0.9)	0
外陰部腟カンジダ症	0	1 (0.3)	0	0
傷害、中毒および処置合併症	0	1 (0.3)	0	0
挫傷	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
傷害、中毒および処置合併症 (Cont.)				
創傷	0	1 (0.3)	0	0
臨床検査	1 (0.6)	30 (8.7)	5 (4.3)	7 (10.3)
アラニンアミノトランスフェラーゼ増加	0	1 (0.3)	1 (0.9)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (0.3)	1 (0.9)	0
血中ビリルビン増加	0	1 (0.3)	0	0
血中クロール減少	0	1 (0.3)	0	0
血中クレアチンホスホキナーゼ増加	0	12 (3.5)	2 (1.7)	3 (4.4)
血中クレアチニン増加	1 (0.6)	2 (0.6)	0	0
クロストリジウム検査陽性	0	0	1 (0.9)	0
γ－グルタミルトランスフェラーゼ増加	0	1 (0.3)	0	0
糸球体濾過率減少	0	0	0	1 (1.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
臨床検査 (Cont.)				
肝酵素上昇	0	1 (0.3)	0	2 (2.9)
眼圧上昇	0	1 (0.3)	0	0
リンパ球数減少	0	2 (0.6)	0	0
リンパ球数増加	0	0	1 (0.9)	0
リンパ球百分率減少	0	1 (0.3)	0	0
好中球数減少	0	9 (2.6)	0	1 (1.5)
血小板数減少	0	1 (0.3)	0	0
トランスアミナーゼ上昇	0	1 (0.3)	0	0
体重増加	0	0	0	1 (1.5)
白血球数減少	0	7 (2.0)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
代謝および栄養障害	1 (0.6)	2 (0.6)	1 (0.9)	0
食欲減退	0	1 (0.3)	0	0
高血糖	1 (0.6)	0	0	0
低ナトリウム血症	0	1 (0.3)	0	0
低リン酸血症	0	0	1 (0.9)	0
筋骨格系および結合組織障害	3 (1.7)	4 (1.2)	1 (0.9)	1 (1.5)
関節痛	0	2 (0.6)	1 (0.9)	1 (1.5)
関節弛緩	0	0	1 (0.9)	0
関節ロック	0	0	1 (0.9)	0
筋痙縮	2 (1.1)	1 (0.3)	0	0
筋骨格系胸痛	0	1 (0.3)	0	0
筋肉痛	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
神経系障害	1 (0.6)	8 (2.3)	0	0
灼熱感	0	1 (0.3)	0	0
脳虚血	0	1 (0.3)	0	0
浮動性めまい	0	1 (0.3)	0	0
頭痛	1 (0.6)	3 (0.9)	0	0
感覚鈍麻	0	1 (0.3)	0	0
片頭痛	0	1 (0.3)	0	0
末梢性ニューロパチー	0	1 (0.3)	0	0
錯感覚	0	1 (0.3)	0	0
精神障害	1 (0.6)	1 (0.3)	0	0
リビドー減退	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
精神障害 (Cont.)				
睡眠障害	1 (0.6)	0	0	0
腎および尿路障害	0	1 (0.3)	0	0
排尿困難	0	1 (0.3)	0	0
生殖系および乳房障害	0	2 (0.6)	1 (0.9)	0
不規則月経	0	1 (0.3)	0	0
月経前頭痛	0	0	1 (0.9)	0
精液変色	0	1 (0.3)	0	0
呼吸器、胸郭および縦隔障害	2 (1.1)	1 (0.3)	0	0
横隔膜痛	1 (0.6)	0	0	0
呼吸困難	0	1 (0.3)	0	0
鼻閉	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
肺塞栓症	1 (0.6)	0	0	0
皮膚および皮下組織障害	2 (1.1)	26 (7.6)	7 (6.0)	1 (1.5)
ざ瘡	1 (0.6)	14 (4.1)	3 (2.6)	0
脱毛症	0	2 (0.6)	0	0
光線過敏性反応	0	1 (0.3)	0	0
そう痒症	1 (0.6)	1 (0.3)	0	0
壊疽性膿皮症	0	1 (0.3)	0	0
発疹	1 (0.6)	4 (1.2)	4 (3.4)	0
紅斑性皮疹	1 (0.6)	0	0	0
斑状丘疹状皮疹	0	1 (0.3)	0	0
丘疹性皮疹	0	2 (0.6)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
皮膚および皮下組織障害 (Cont.)				
酒さ	0	0	0	1 (1.5)
脂漏性皮膚炎	0	1 (0.3)	0	0
皮膚病変	0	1 (0.3)	0	0
皮膚潰瘍	0	0	1 (0.9)	0
毛細血管拡張症	0	0	0	1 (1.5)
血管障害	1 (0.6)	0	1 (0.9)	1 (1.5)
潮紅	0	0	0	1 (1.5)
骨盤静脈血栓症	1 (0.6)	0	0	0
血栓性静脈炎	0	0	1 (0.9)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表4

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3__1.3.3

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
Any adverse event	7 (4.0)	9 (2.6)	2 (1.7)	0
血液およびリンパ系障害	0	1 (0.3)	0	0
リンパ球減少症	0	1 (0.3)	0	0
胃腸障害	6 (3.4)	3 (0.9)	0	0
大腸炎	1 (0.6)	0	0	0
潰瘍性大腸炎	4 (2.3)	3 (0.9)	0	0
下痢	0	1 (0.3)	0	0
血性下痢	0	1 (0.3)	0	0
大腸穿孔	1 (0.6)	0	0	0
感染症および寄生虫症	0	1 (0.3)	1 (0.9)	0
COVID－19肺炎	0	1 (0.3)	1 (0.9)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
臨床検査	0	4 (1.2)	0	0
血中クレアチンホスホキナーゼ増加	0	1 (0.3)	0	0
血中リン減少	0	1 (0.3)	0	0
ヘモグロビン減少	0	1 (0.3)	0	0
好中球数減少	0	1 (0.3)	0	0
神経系障害	1 (0.6)	0	0	0
頭痛	1 (0.6)	0	0	0
呼吸器、胸郭および縦隔障害	0	0	1 (0.9)	0
慢性閉塞性肺疾患	0	0	1 (0.9)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表5

[redacted]20[redacted] 16:30 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.3.1

Subjects with Treatment-Emergent Adverse Events Leading to Death
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
Any adverse event	0	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表6

[redacted]20[redacted] 16:30 <[redacted] >
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3__2.1.1

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
Any adverse event	8 (4.5)	11 (3.2)	4 (3.4)	1 (1.5)
血液およびリンパ系障害	1 (0.6)	1 (0.3)	0	0
貧血	1 (0.6)	1 (0.3)	0	0
胃腸障害	5 (2.8)	4 (1.2)	2 (1.7)	1 (1.5)
腹部不快感	0	0	1 (0.9)	0
下腹部痛	0	0	1 (0.9)	0
大腸炎	1 (0.6)	0	0	0
潰瘍性大腸炎	3 (1.7)	4 (1.2)	1 (0.9)	1 (1.5)
大腸穿孔	1 (0.6)	0	0	0
一般・全身障害および投与部位の状態	0	1 (0.3)	0	0
胸痛	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
感染症および寄生虫症	1 (0.6)	2 (0.6)	1 (0.9)	0
COVID－19肺炎	0	1 (0.3)	1 (0.9)	0
デング熱	0	1 (0.3)	0	0
腸球菌感染	1 (0.6)	0	0	0
大腸菌感染	1 (0.6)	0	0	0
傷害、中毒および処置合併症	1 (0.6)	1 (0.3)	0	0
消化管ストーマ壊死	1 (0.6)	0	0	0
手骨折	0	1 (0.3)	0	0
代謝および栄養障害	0	1 (0.3)	0	0
栄養障害	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
精神障害	0	1 (0.3)	0	0
急性精神病	0	1 (0.3)	0	0
呼吸器、胸郭および縦隔障害	1 (0.6)	0	1 (0.9)	0
慢性閉塞性肺疾患	0	0	1 (0.9)	0
肺塞栓症	1 (0.6)	0	0	0
皮膚および皮下組織障害	1 (0.6)	0	0	0
壊疽性膿皮症	1 (0.6)	0	0	0
血管障害	1 (0.6)	0	0	0
骨盤静脈血栓症	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表7

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3__2.2.1

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
Any adverse event	9 (5.1)	6 (1.7)	2 (1.7)	2 (2.9)
血液およびリンパ系障害	0	1 (0.3)	0	0
リンパ球減少症	0	1 (0.3)	0	0
耳および迷路障害	0	1 (0.3)	0	0
耳鳴	0	1 (0.3)	0	0
眼障害	0	1 (0.3)	0	0
霧視	0	1 (0.3)	0	0
胃腸障害	6 (3.4)	3 (0.9)	1 (0.9)	2 (2.9)
潰瘍性大腸炎	5 (2.8)	3 (0.9)	1 (0.9)	2 (2.9)
大腸穿孔	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.2.1

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=177) n (%)	UPA 45 mg QD (N=344) n (%)	Placebo/ UPA 45 mg QD (N=116) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
一般・全身障害および投与部位の状態	1 (0.6)	0	1 (0.9)	0
無力症	1 (0.6)	0	0	0
疲労	1 (0.6)	0	0	0
発熱	0	0	1 (0.9)	0
感染症および寄生虫症	1 (0.6)	0	0	0
腸球菌感染	1 (0.6)	0	0	0
大腸菌感染	1 (0.6)	0	0	0
傷害、中毒および処置合併症	1 (0.6)	0	0	0
消化管ストーマ壊死	1 (0.6)	0	0	0
筋骨格系および結合組織障害	0	2 (0.6)	0	0
関節痛	0	1 (0.3)	0	0
関節炎	0	1 (0.3)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.2.1

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=177) n (%)	Part 1 UPA 45 mg QD (N=344) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=116) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=68) n (%)
筋骨格系および結合組織障害 (Cont.)				
弾発指	0	1 (0.3)	0	0
神経系障害	2 (1.1)	1 (0.3)	0	0
灼熱感	0	1 (0.3)	0	0
頭痛	1 (0.6)	0	0	0
片頭痛	1 (0.6)	0	0	0
呼吸器、胸郭および縦隔障害	1 (0.6)	0	0	0
肺塞栓症	1 (0.6)	0	0	0
皮膚および皮下組織障害	0	0	1 (0.9)	0
発疹	0	0	1 (0.9)	0
血管障害	1 (0.6)	0	0	0
骨盤静脈血栓症	1 (0.6)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表8

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.1_J

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1			Part 2	
	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Difference UPA - Placebo (95% CI&)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Subjects with:					
Any adverse event (AE)	11 (37.9)	32 (61.5)	23.6 (1.5, 45.7)	9 (45.0)	4 (57.1)
Any AE with reasonable possibility of being related to study drug$	0	17 (32.7)	32.7 (19.9, 45.4)	2 (10.0)	2 (28.6)
Any severe AE	1 (3.4)	2 (3.8)	0.4 (-8.1, 8.8)	0	0
Any serious AE	2 (6.9)	2 (3.8)	-3.1 (-13.7, 7.6)	0	0
Any AE leading to discontinuation of study drug	1 (3.4)	1 (1.9)	-1.5 (-9.1, 6.1)	0	0
Any AE leading to death	0	0	0.0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
& 95% CI for treatment difference is based on the normal approximation.

Program Source Code: [redacted]

TABLE 14.3 1.1.1 J

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1			Part 2	
	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Difference UPA - Placebo (95% CI&)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Subjects with:					
Deaths#	0	0	0.0	0	0
Occurring <= 30 days after last dose	0	0	0.0	0	0
Occurring > 30 days after last dose	0	0	0.0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
& 95% CI for treatment difference is based on the normal approximation.

Program Source Code: [redacted]

表9

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3__1.2.1.1_J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	11 (37.9)	32 (61.5)	9 (45.0)	4 (57.1)
血液およびリンパ系障害	0	5 (9.6)	0	0
リンパ球減少症	0	1 (1.9)	0	0
好中球減少症	0	4 (7.7)	0	0
眼障害	1 (3.4)	1 (1.9)	0	0
結膜出血	0	1 (1.9)	0	0
翼状片	1 (3.4)	0	0	0
胃腸障害	5 (17.2)	8 (15.4)	1 (5.0)	0
潰瘍性大腸炎	2 (6.9)	0	0	0
便秘	1 (3.4)	1 (1.9)	0	0
齲歯	1 (3.4)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=29) n (%)	Part 1 UPA 45 mg QD (N=52) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=20) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
胃腸障害 (Cont.)				
歯肉腫脹	0	1 (1.9)	0	0
痔核	0	1 (1.9)	0	0
胃酸過多	0	1 (1.9)	0	0
歯周病	0	1 (1.9)	0	0
肛門周囲痛	0	1 (1.9)	0	0
口内炎	1 (3.4)	4 (7.7)	1 (5.0)	0
一般・全身障害および投与部位の状態	2 (6.9)	5 (9.6)	0	0
胸痛	0	1 (1.9)	0	0
末梢性浮腫	1 (3.4)	0	0	0
発熱	1 (3.4)	4 (7.7)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=29) n (%)	Part 1 UPA 45 mg QD (N=52) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=20) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
肝胆道系障害	0	1 (1.9)	0	0
肝機能異常	0	1 (1.9)	0	0
感染症および寄生虫症	2 (6.9)	13 (25.0)	4 (20.0)	2 (28.6)
気管支炎	0	1 (1.9)	0	0
サイトメガロウイルス性大腸炎	0	1 (1.9)	0	0
毛包炎	0	3 (5.8)	0	0
単純ヘルペス	0	1 (1.9)	0	0
麦粒腫	0	0	1 (5.0)	0
インフルエンザ	0	1 (1.9)	2 (10.0)	0
上咽頭炎	2 (6.9)	3 (5.8)	0	0
口腔ヘルペス	0	2 (3.8)	1 (5.0)	0
歯周炎	0	0	1 (5.0)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=29) n (%)	Part 1 UPA 45 mg QD (N=52) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=20) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
感染症および寄生虫症 (Cont.)				
咽頭炎	0	0	0	1 (14.3)
肺炎	0	1 (1.9)	0	0
腎盂腎炎	0	1 (1.9)	0	0
白癬感染	0	0	0	1 (14.3)
上気道感染	0	1 (1.9)	0	0
臨床検査	0	9 (17.3)	2 (10.0)	3 (42.9)
アラニンアミノトランスフェラーゼ増加	0	1 (1.9)	1 (5.0)	0
アミラーゼ増加	0	1 (1.9)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (1.9)	1 (5.0)	0
血中クレアチンホスホキナーゼ増加	0	4 (7.7)	1 (5.0)	2 (28.6)
血中尿酸増加	0	0	1 (5.0)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
臨床検査 (Cont.)				
γ-グルタミルトランスフェラーゼ増加	0	1 (1.9)	0	0
好中球数減少	0	4 (7.7)	0	1 (14.3)
体重増加	0	0	0	1 (14.3)
白血球数減少	0	1 (1.9)	0	0
代謝および栄養障害	1 (3.4)	2 (3.8)	0	0
高尿酸血症	1 (3.4)	1 (1.9)	0	0
栄養障害	0	1 (1.9)	0	0
筋骨格系および結合組織障害	2 (6.9)	4 (7.7)	1 (5.0)	0
関節痛	0	0	1 (5.0)	0
関節炎	0	2 (3.8)	0	0
関節障害	1 (3.4)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=29) n (%)	Part 1 UPA 45 mg QD (N=52) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=20) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
筋骨格系および結合組織障害 (Cont.)				
側腹部痛	0	1 (1.9)	0	0
筋肉痛	0	1 (1.9)	0	0
変形性関節症	1 (3.4)	0	0	0
弾発指	0	1 (1.9)	0	0
神経系障害	1 (3.4)	3 (5.8)	0	0
頭痛	0	2 (3.8)	0	0
末梢性ニューロパチー	0	1 (1.9)	0	0
失神寸前の状態	1 (3.4)	0	0	0
味覚障害	0	1 (1.9)	0	0
精神障害	1 (3.4)	0	0	0
不眠症	1 (3.4)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=29) n (%)	Part 1 UPA 45 mg QD (N=52) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=20) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
生殖系および乳房障害	0	1 (1.9)	0	0
無月経	0	1 (1.9)	0	0
呼吸器、胸郭および縦隔障害	0	1 (1.9)	0	0
口腔咽頭痛	0	1 (1.9)	0	0
皮膚および皮下組織障害	2 (6.9)	11 (21.2)	3 (15.0)	1 (14.3)
ざ瘡	0	6 (11.5)	2 (10.0)	0
脱毛症	0	0	0	1 (14.3)
湿疹	1 (3.4)	1 (1.9)	0	0
そう痒症	0	1 (1.9)	0	0
壊疽性膿皮症	1 (3.4)	0	0	0
発疹	0	1 (1.9)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=29) n (%)	Part 1 UPA 45 mg QD (N=52) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=20) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
皮膚および皮下組織障害 (Cont.)				
脂漏性皮膚炎	0	2 (3.8)	1 (5.0)	0
血管障害	0	1 (1.9)	0	1 (14.3)
本態性高血圧症	0	0	0	1 (14.3)
ほてり	0	1 (1.9)	0	0
高血圧	0	1 (1.9)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表10

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 3

TABLE 14.3__1.3.1.1_J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	0	17 (32.7)	2 (10.0)	2 (28.6)
血液およびリンパ系障害	0	4 (7.7)	0	0
好中球減少症	0	4 (7.7)	0	0
胃腸障害	0	2 (3.8)	0	0
痔核	0	1 (1.9)	0	0
口内炎	0	1 (1.9)	0	0
一般・全身障害および投与部位の状態	0	1 (1.9)	0	0
発熱	0	1 (1.9)	0	0
感染症および寄生虫症	0	1 (1.9)	0	0
肺炎	0	1 (1.9)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
臨床検査	0	7 (13.5)	1 (5.0)	2 (28.6)
アラニンアミノトランスフェラーゼ増加	0	1 (1.9)	1 (5.0)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (1.9)	1 (5.0)	0
血中クレアチンホスホキナーゼ増加	0	2 (3.8)	0	1 (14.3)
γ-グルタミルトランスフェラーゼ増加	0	1 (1.9)	0	0
好中球数減少	0	4 (7.7)	0	1 (14.3)
体重増加	0	0	0	1 (14.3)
白血球数減少	0	1 (1.9)	0	0
神経系障害	0	1 (1.9)	0	0
頭痛	0	1 (1.9)	0	0
末梢性ニューロパチー	0	1 (1.9)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
皮膚および皮下組織障害	0	5 (9.6)	1 (5.0)	0
ざ瘡	0	3 (5.8)	1 (5.0)	0
発疹	0	1 (1.9)	0	0
脂漏性皮膚炎	0	1 (1.9)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表11

[redacted]20[redacted] 09:05 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3__1.3.3_J

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	1 (3.4)	2 (3.8)	0	0
胃腸障害	1 (3.4)	0	0	0
潰瘍性大腸炎	1 (3.4)	0	0	0
臨床検査	0	2 (3.8)	0	0
血中クレアチンホスホキナーゼ増加	0	1 (1.9)	0	0
好中球数減少	0	1 (1.9)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表12

[redacted]20[redacted] 09:05 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.3.1_J

Subjects with Treatment-Emergent Adverse Events Leading to Death
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	0	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表13

[redacted]20[redacted] 09:05 <[redacted] >
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3__2.1.1_J

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Part 1 Placebo (N=29) n (%)	Part 1 UPA 45 mg QD (N=52) n (%)	Part 2 Placebo/ UPA 45 mg QD (N=20) n (%)	Part 2 UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	2 (6.9)	2 (3.8)	0	0
胃腸障害	1 (3.4)	0	0	0
潰瘍性大腸炎	1 (3.4)	0	0	0
一般・全身障害および投与部位の状態	0	1 (1.9)	0	0
胸痛	0	1 (1.9)	0	0
代謝および栄養障害	0	1 (1.9)	0	0
栄養障害	0	1 (1.9)	0	0
皮膚および皮下組織障害	1 (3.4)	0	0	0
壊疽性膿皮症	1 (3.4)	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

Program Source Code: [redacted]

表14

[redacted]20[redacted] 09:05 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.2.1_J

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1 Population and SA2 Population - Japan Analysis Set)

	Part 1		Part 2	
MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=29) n (%)	UPA 45 mg QD (N=52) n (%)	Placebo/ UPA 45 mg QD (N=20) n (%)	UPA 45 mg QD/ UPA 45 mg QD (N=7) n (%)
Any adverse event	1 (3.4)	1 (1.9)	0	0
胃腸障害	1 (3.4)	0	0	0
潰瘍性大腸炎	1 (3.4)	0	0	0
筋骨格系および結合組織障害	0	1 (1.9)	0	0
関節炎	0	1 (1.9)	0	0
弾発指	0	1 (1.9)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) for Part 1 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 1 and within 30 days after the last dose administration of the study drug for subjects who are not enrolled in Part 2 and do not participate the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in Part 2 if the subject is enrolled into Part 2 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.
Treatment-emergent AEs (TEAEs) for Part 2 are defined as events that begin or worsen either on or after the first dose of the study drug in Part 2 and within 30 days after the last dose administration of the study drug for subjects who do not participate in the Maintenance Study M14-234 Substudy 3 and M14-533 or until first dose of study drug in the Maintenance Study M14-234 Substudy 3 if the subject is enrolled into Maintenance Study M14-234 Substudy 3 or until first dose of study drug in M14-533 if the subject is enrolled into M14-533.

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
デング熱	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:UPADACITINIB 45 MG QD	4[redacted]	MALE	WHITE

Medical History	Onset Year
C. DIFFICILE	20[redacted]
LEFT SIDED UC	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: VIDEOCOLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPADACITINIB 45 MG QD	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MERCAPTOPURINE	50 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
MEPREDNISONE	10 mg	QD	Y-M: 20[redacted] / -105
MESALAZINE	1 g	QD	Y-M: 20[redacted] / -99
GANCICLOVIR	370 mg	BID	Y-M: 20[redacted] / -54
HYDROCORTISONE	100 mg	QID	Y-M: 20[redacted] / -56
CALCIUM	950 mg	QD	Y-M: 20[redacted] / -49
MEPREDNISONE	20 mg	QD	Y-M: 20[redacted] / -49
SULFAMETHOXAZOLE;TRIMETHOPRIM	160/800 mg	OTHER: 3 TIMES A WEEK	Y-M: 20[redacted] / -49
MEPREDNISONE	20 mg	QD	Y-M: 20[redacted] / -15
INFLUENZA VACCINE	0.5 mL	OTHER: 1 TIME	Y-M: 20[redacted] / -5
FENTANYL	75 mg	OTHER: ONCE	Y-M: 20[redacted] / -8
PROPOFOL	100 mg	OTHER: ONCE FOR ENDOSCOPY	Y-M: 20[redacted] / -8
MACROGOL	4 L	OTHER: 1 TIME	Y-M: 20[redacted] / -9
BCG VACCINE	NOT REPORTED	NOT REPORTED	Y: 19[redacted]
MESALAZINE	2 g	BID	Y: 20[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY WEEK	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CALCIUM	950 mg	QD	Y-M: 20[redacted] / -49	ONGOING

SULFAMETHOXAZOLE;TRIMETHOPRIM	160/800 mg	OTHER: 3 TIMES A WEEK	Y-M: 20[redacted] / -49	ONGOING
MEPREDNISONE	20 mg	QD	Y-M: 20[redacted] / -15	Y-M: 20[redacted] / 28
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 35
HYDROCORTISONE	50 mg	TID	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 30
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 35
PARACETAMOL	1 g	TID	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 35
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 31
MEPREDNISONE	20 mg	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 59
CETIRIZINE	10 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 35
MESALAZINE	2 g	BID	Y: 20[redacted]	ONGOING

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

Event Description	DENGUE VIRUS
Preferred term	デング熱
AE Onset Date / Rx Day	[redacted]20[redacted] / 28
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted](RX DAY 28): Platelets: 203 [150 - 410] 10^9/L; [redacted]20[redacted](RX DAY 29): Platelets: 190 [150 - 410] 10^9/L; [redacted]20[redacted](RX DAY 30): Platelets: 157 [150 - 410] 10^9/L; [redacted]20[redacted](RX DAY 31): Platelets: 120 [150 - 410] 10^9/L; [redacted]20[redacted](RX DAY 32): Platelets: 105 [150 - 410] 10^9/L; [redacted]20[redacted](RX DAY 33): Platelets: 108 [150 - 410] 10^9/L; [redacted]20[redacted](RX DAY 34): Platelets: 145 [150 - 410] 10^9/L

Microbiology

[redacted]20[redacted](RX DAY 28): OTHER NASOPHARYNGEAL SWAB NPTST034-COVID 19 PCR: NEGATIVE; OTHER NASOPHARINGEAL SWAB NPTST087-RESPIRATORY PANEL: NEGATIVE; [redacted]20[redacted](RX DAY 29): BLOOD NPTST019-BLOOD CULTURE: NEGATIVE; [redacted]20[redacted](RX DAY 31): STOOL NPTST028-CLOSTRIDIUM DIFFICILE: NEGATIVE; STOOL NPTST052-GDH: NEGATIVE; STOOL NPTST093-STOOL CULTURE: NEGATIVE; [redacted]20[redacted](RX DAY 34): BLOOD NPTST074-NS1 ANTIGEN: POSITIVE-DENGUE FEVER; [redacted]20[redacted](RX DAY 42): BLOOD NPTST061-IGM FOT DENGUE: POSITIVE-DENGUE INFECTION

SAE Supplemental Procedure

[redacted]20[redacted](RX DAY 28): TORAX X RAY: NO PARTICULARY FINDINGS;[redacted]20[redacted](RX DAY 30): CHEST COMPUTED TOMOGRAPHY: NORMAL

AE Stopped Rx Day	46
Duration of AE	19 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DENGUE INFECTION
Discontinued Study Drug Due to the Event	NO

SAE Criteria HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:19:49
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-675

治験責任医師からの報告。本被験者はアルゼンチンの 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，デングウイルスの事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与28日後＊ ，被験者はデングウイルスを発現した。投与46日後＊ ，デングウイルスは消失した。

投与28日後＊ ，被験者は発熱があり入院した。被験者の妻がデングウイルスに感染していた。被験者は，入院当初の 4 日間は発熱し，重症急性呼吸器症候群コロナウイルス-2（SARS-CoV-2）の予防隔離を行った。被験者は診断的検査及び臨床検査を受けた。入院 5 日目に皮膚に発疹が現れ，入院 8 日目に消失した。投与35日後＊，被験者は回復し，退院した。
投与45日後＊，被験者は無症状であった。

投与された薬剤は，パラセタモール，オメプラゾール，meprednisone，ヒドロコルチゾン，エノキサパリン及びセチリジンであった。

The patient's past medications include:

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

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

METHOTREXATE for ARTHRALGIA (20[redacted]- 20[redacted])

INFLIXIMAB ([redacted] 20[redacted]- [redacted] 20[redacted])

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

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

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

FLU VACCINE for PROPHYLAXSIS ([redacted] 20[redacted]-[redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Dengue fever virus infection (10012312) (Dengue fever (10012310)) [v.23.1] [10012312]

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 DENGUE VIRUS

- Investigator: Dengue infection

- AbbVie: Event is more likely related to Argentina's current outbreak of Dengue fever.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] 20[redacted] **CHEST COMPUTED TOMORGRAPHY:** Normal

[redacted] 20[redacted] **CLOSTRIDIUM DIFFICILE STOOL:** NEGATIVE

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

[redacted] 20[redacted] **IGM FOR DENGUE:** Positive; dengue infection

[redacted] 20[redacted] **NASOPHARYNGEAL SWAB:** RESPIRATORY PANEL; NEGATIVE

[redacted] **20[redacted]NS1 ANTIGEN:** Positive - Dengue Fever

[redacted] **20[redacted]PLATELET COUNT:** 203 10^3/uL (normal 150 to 410)

[redacted] **20[redacted]PLATELET COUNT:** 190 10^3/uL (normal 150 to 410)

[redacted] **20[redacted]PLATELET COUNT:** 157 10^3/uL (normal 150 to 410)

[redacted] **20[redacted]PLATELET COUNT:** 120 10^3/uL (normal 150 to 410)

[redacted] **20[redacted]PLATELET COUNT:** 105 10^3/uL (normal 150 to 410)

[redacted] **20[redacted]PLATELET COUNT:** 108 10^3/uL (normal 150 to 410)

[redacted] **20[redacted]PLATELET COUNT:** 145 10^3/uL (normal 150 to 410)

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

[redacted] **20[redacted]STOOL GDH:** Negative

[redacted] **20[redacted]THORAX X RAY:** NO PARTICULARY FINDINGS

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
急性精神病	X			

Treatment Group	Age at Study Start	Sex	Race
P1:UPADACITINIB 45 MG QD	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ACUTE PSYCHOTIC EPISODE	20[redacted]
ANAEMIA	NOT REPORTED
EXTENSIVE UC/PANCOLITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0 PACK	3	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPADACITINIB 45 MG QD	45 mg	ORAL	QD	[redacted]20[redacted]/ 1	[redacted]20[redacted]/ 55	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
GOLIMUMAB	100 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
ETHINYLESTRADIOL;NORELGESTROMIN	203 ug	OTHER: EVERY WEEK	Y-M: 20[redacted] / -10
PROPOFOL	150 mg	OTHER: ONCE	Y-M: 20[redacted] / -11
SODIUM PHOSPHATE	130 mL	QD	Y-M: 20[redacted] / -12
PARACETAMOL	500 mg	PRN	Y: 20[redacted]
MEBEVERINE	200 mg	BID	Y: 20[redacted]
METAMIZOLE	20 gtt	PRN	Y: 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
ETHINYLESTRADIOL; NORELGESTROMIN	203 ug	OTHER: EVERY WEEK	Y-M: 20[redacted] / -10	Y-M: 20[redacted] / 8
PROPOFOL	150 mg	OTHER: ONCE	Y-M: 20[redacted] / -11	Y-M: 20[redacted] / -11
SODIUM PHOSPHATE	130 mL	QD	Y-M: 20[redacted] / -12	Y-M: 20[redacted] / -11
OLANZAPINE	10 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 19
OLANZAPINE	5 mg	QD	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 22
OLANZAPINE	2.5 mg	QD	Y-M: 20[redacted] / 23	ONGOING
ETHINYLESTRADIOL; ETONOGESTREL	1 OTHER: VAGINAL RING	OTHER: FOR THREE WEEKS, THEN ONE WEEK PAUSE	Y-M: 20[redacted] / 9	ONGOING
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 55
PROPOFOL	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 55
SODIUM PHOSPHATE	130 mL	QD	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 55
PARACETAMOL	500 mg	PRN	Y: 20[redacted]	ONGOING
MEBEVERINE	200 mg	BID	Y: 20[redacted]	ONGOING
METAMIZOLE	20 gtt	PRN	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	ACUTE PSYCHOTIC EPISODE
Preferred term	急性精神病
AE Onset Date / Rx Day	[redacted]20[redacted] / 4
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 16): Blood Urea Nitrogen: 2.712972 [2.14182 - 7.1394] MMOL/L; Creatinine: 68.07051 [44.20163 - 79.562934] UMOL/L; [redacted]20[redacted] (RX DAY 18): NPTST001-6-MAM: NEGATIVE [0 - 10] ng/mL; NPTST008-AMPHETAMINE: NEGATIVE [0 - 1000] ng/mL; NPTST017-BARBITURATE: NEGATIVE [0 - 200] ng/mL; NPTST018-BENZODIAZEPINE: NEGATIVE [0 - 200] ng/mL; NPTST020-BUPRENORPHIN: NEGATIVE [0 - 100] ng/mL; NPTST025-CANNABINOIDE: NEGATIVE [0 - 100] ng/mL; NPTST033-COCAINE: NEGATIVE [0 - 300] ng/mL; NPTST040-EDDP: NEGATIVE [0 - 100] ng/mL; NPTST071-METHADON: NEGATIV [0 - 300] ng/mL; NPTST075-OPIATE: NEGATIVE [0 - 300] ng/mL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	POTENTIALLY DUE TO HORMONAL CONTRACEPTIVE PATCH
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:19:49

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-675

治験責任医師からの報告。本被験者はオーストリアの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性精神病発作の事象を発現した。関連する病歴は，元喫煙者（1 日 1 本を 3 年間），急性精神病発作，現飲酒者（1 日 2 杯未満），及び精神病性の統合失調症（叔母）の家族歴であった。